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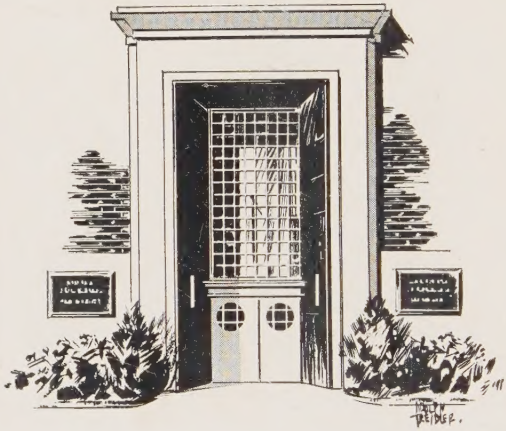

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ORGANIC SYNTHESES

AN ANNUAL PUBLICATION OF SATISFACTORY METHODS FOR THE PREPARATION OF ORGANIC CHEMICALS

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PREFACE TO VOLUME IV

THE general plan outlined in the first volume of the series has been followed in the subsequent publications; but it has been found advisable to include preparations which are carried out on a somewhat reduced scale, since the carefully described directions have found application not merely in the semi-commercial preparation of needed research chemicals and reagents but also in the instruction of graduate students entering the organic field. However, it is the experience of the editors that the reduction of preparations described on a large scale is usually less difficult than the reverse procedure.

The sections on "Other Methods of Preparation" are not intended to include all possible methods but rather those that are of interest chiefly from the preparative standpoint. The Cumulative Index, started with Volume III, is being continued.

The friendly cooperation of other workers in Organic Chemistry has been gratifying, and the editors again cordially invite contributions from any investigator who has occasion to study an organic preparation exhaustively enough to justify the presentation of certified directions.

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ORGANIC SYNTHESES

I

ACETYL MANDELYL CHLORIDE

$$C_6H_5CHOHCO_2H + CH_3COCl \rightarrow C_6H_5CH(OCOCH_3)CO_2H + HCl$$

$$C_6H_5CH(OCOCH_3)CO_2H + SOCl_2 \rightarrow C_6H_5CH(OCOCH_3)COCl + SO_2 + HCl$$

Prepared by F. K. Thayer.
Checked by Roger Adams and E. E. Dreger.

1. Procedure

In a 500-cc. Claisen distilling flask with a low side-tube connected to a condenser, are placed 105 g. of mandelic acid (m.p. 118°) and 151 g. of acetyl chloride. A reaction sets in without the application of heat (Note 1). As soon as a clear solution results, the flask is warmed on a water bath and the excess acetyl chloride is distilled. The last trace of acetyl chloride may be removed by prolonged drying in a vacuum. The acetyl mandelic acid then crystallizes in large, round, white clusters after one or two days' standing. The yield is 130–133 g. (97–99 per cent of the theoretical amount) (Note 2).

To the crude acetyl mandelic acid still containing some acetyl chloride obtained as described above, is added 250 g. of thionyl chloride. The reaction starts at once without warming but it is necessary to reflux for four hours to complete the reaction (Note 3). The excess thionyl chloride is then distilled

and the residue distilled in a vacuum (Note 4). The yield is 115–120 g. (79–83 per cent of the theoretical amount) of almost colorless liquid boiling at 125–130°/10 mm. (150–155°/33 mm.).

2. Notes

1. Occasionally the application of a little heat is necessary to bring about a more rapid acetylation.

2. The melting points given in the literature range from 39 to 80°. The acetyl mandelic acid is difficult to crystallize but may be purified from benzene or chloroform, preferably the former. The product thus obtained melts at about 79–80°.

3. Prolonged refluxing of the acetylated mandelic acid with the thionyl chloride tends to lower the yield.

4. Anschütz gives the boiling point of acetyl mandelyl chloride as 129°/10 mm. The vacuum used should be as low as possible, to avoid the formation of tar during the distillation.

3. Other Methods of Preparation

Acetyl mandelic acid was described by Naquet and Louguinine,[1] but their product has been shown to be contaminated with the ethyl ester of acetyl mandelic acid. Dupont [2] obtained the compound by the oxidation of diacetyl 1, 4-diphenylbutine-2-diol-1, 4. Anschütz and Böcker [3] prepared acetyl mandelic acid, and from it the acid chloride, by the use of phosphorus pentachloride, but with poor yields. Von Braun and Müller [4] state that acetyl mandelyl chloride can be made from acetylated mandelic acid and thionyl chloride, the resulting product being a viscous yellow oil.

[1] Compt. rend. **62**, 430 (1866); Ann. **139**, 302 (1866).
[2] Compt. rend. **150**, 1525 (1910).
[3] Ann. **368**, 57, 59 (1909).
[4] Ber. **51**, 244 (1918).

II

α-AMINO-*n*-CAPROIC ACID

$$CH_3(CH_2)_3CHBrCO_2H + 2NH_3 \rightarrow CH_3(CH_2)_3CHNH_2CO_2H + NH_4Br$$

Prepared by C. S. Marvel and V. du Vigneaud.
Checked by H. T. Clarke and E. R. Taylor.

1. Procedure

In a 1-l. round-bottom flask is placed 760 g. of concentrated ammonium hydroxide (sp. gr. 0.9) and to this is slowly added 150 g. of α-bromocaproic acid (Note 1). The flask is well stoppered and allowed to stand in a warm place (50–55°) for twenty to thirty hours. The amino acid separates and is filtered off with suction and washed with methyl alcohol (Note 2). This crop of crystals weighs 51–56 g. The aqueous filtrate is evaporated nearly to dryness on a steam bath and then treated with about 250 cc. of methyl alcohol. This precipitates a second crop of amino acid contaminated with ammonium bromide. On washing with methyl alcohol and recrystallizing from water, there is obtained 10–15 g. more of pure product. The total yield is 63–68 g. (62–67 per cent of the theoretical amount).

2. Notes

1. The once-distilled bromocaproic acid (p. 9) is satisfactory.

2. If the amino acid is not carefully washed with alcohol, it contains ammonium bromide and may possess an objectionable

odor. Methyl alcohol is preferable to ethyl alcohol since it dissolves ammonium bromide more readily.

3. Other Methods of Preparation

α-Amino-*n*-caproic acid has been prepared by the action of ammonia on α-bromo-*n*-caproic acid.[1]

[1] J. prakt. Chem. (2) **1**, 7 (1870); Ber. **33**, 2381 (1900); Z. physiol. Chem. **86**, 456 (1913); J. Am. Chem. Soc. **42**, 320 (1920).

III

ARSONO- AND ARSENOACETIC ACIDS

$$ClCH_2CO_2Na + Na_3AsO_3 \rightarrow NaCl + CH_2(CO_2Na)AsO_3Na_2$$

$$2CH_2(CO_2H)AsO_3H_2 + 8H(H_3PO_2) \rightarrow \begin{matrix} AsCH_2CO_2H \\ \| \\ AsCH_2CO_2H \end{matrix} + 6H_2O$$

Prepared by C. S. Palmer.
Checked by Oliver Kamm.

1. Procedure

One hundred grams of powdered arsenious oxide is added to the hot solution obtained by dissolving 160 g. of sodium hydroxide in 300 cc. of water. After the solution has cooled to 20°, 48 g. of chloroacetic acid is added. The suspension is well stirred during about five minutes, when a strongly exothermic reaction begins, the temperature rises to 70–75°, and a clear solution results.

The reaction mixture is permitted to stand at room temperature during one hour, or longer if desired (Note 1). The solution is acidified with 160 cc. of glacial acetic acid and, after the temperature has been lowered to 40° by cooling, the precipitated arsenious oxide is filtered off by suction and washed with 50 cc. of water.

The filtrate is poured into a solution containing 185 g. of crystallized barium chloride dissolved in 600 cc. of hot water. Barium arsonoacetate, $Ba(O_2CCH_2AsO_3Ba)_2$ (hydrated), forms a thick, finely divided precipitate. The mixture is stirred for several minutes and then allowed to stand until the following day, when it is filtered upon a 15-cm. Büchner funnel and washed

thoroughly with water (Note 2). The yield of air-dry * product is 220 g. (96 per cent of the theoretical amount).

Sodium arsonoacetate is prepared by adding the freshly filtered and washed barium arsonoacetate as obtained above (without drying) to a solution of 108 g. of anhydrous sodium sulfate in 500 cc. of hot water. The mixture is mechanically stirred for one hour, the barium sulfate filtered off, and the filtrate concentrated on the steam bath until crystallization commences. Upon cooling and stirring (Note 3), sodium arsonoacetate separates and is filtered by suction, the filtrate being concentrated to obtain a second crop of crystals. The yield of the combined fractions is 100–110 g. (80–88 per cent of the theoretical amount).

A solution of 12.5 g. of sodium arsonoacetate and 30 g. of sodium hypophosphite ($NaH_2PO_2 \cdot H_2O$) in 150 cc. of cold 15 per cent sulfuric acid is allowed to stand at room temperature. After two or three days, the yellow precipitate is filtered off, washed with water, and dried in a vacuum over sulfuric acid or phosphorus pentoxide. A second crop is obtained by allowing the mother liquid to stand for two days longer.

The arsenoacetic acid consists of minute yellow needles, which do not melt below 260° although they undergo considerable decomposition above 200°. The yield is 5 g. (74 per cent of the theoretical amount).

2. Notes

1. The reaction between sodium arsenite and chloroacetic acid is very rapid, as may easily be demonstrated by titrating 1-cc. portions of the solution with N/10 iodine, according to the usual volumetric method for arsenious acid, before and after the reaction with chloroacetic acid. The excess of sodium arsenite is necessary, as was learned by means of an iodometric study of the reaction.

* The air-dry sample contains 13 per cent of water of hydration, as determined by actual analysis.

2. If the thick paste is not allowed to stand over night, filtration is more cumbersome and it is extremely difficult to wash the precipitate free from arsenites. With this precaution, it is found that after five washings with 250-cc. portions of water, the final filtrate, as well as the desired barium salt, is practically free from iodine-reducing compounds.

3. Stirring is required during the crystallization process, since otherwise the product tends to form a solid cake. The sodium salt is obtained without water of crystallization. Usually, it contains a trace of sulfate but this does not interfere with its subsequent use. The sulfate may be removed by recrystallization from water.

3. Other Methods of Preparation

Arsonoacetic acid was obtained by Ehrlich and Bertheim [1] by treating *p*-aminophenylarsenoacetic acid with bromine. It has been prepared by the action of three molecular equivalents of sodium chloroacetate on two of sodium arsenite, followed by isolation as the calcium salt,[2] but it is found that these proportions are less satisfactory than the ones adopted.[3] Arsenoacetic acid has been prepared recently by Palmer.[3]

[1] Ber. **43**, 926 (1910).
[2] U. S. Pat. 1,445,685; Austrian Pat. 93,325; Swiss Pat. 97,977.
[3] J. Am. Chem. Soc. **45**, 3023 (1923).

IV

α-BROMO-*n*-CAPROIC ACID

$$CH_3(CH_2)_4CO_2H + Br_2(PCl_3) \rightarrow CH_3(CH_2)_3CHBrCO_2H + HBr$$

Prepared by H. T. Clarke and E. R. Taylor.
Checked by C. S. Marvel and R. L. Shriner.

1. Procedure

Two hundred grams of freshly distilled dry *n*-caproic acid is placed in a 1-l. flask with 300 g. of bromine which has been dried by washing once with 200 cc. of concentrated sulfuric acid (Note 1). A 3-cc. portion of phosphorus trichloride is cautiously added and the flask connected to a reflux condenser (Note 2), the top of which is connected with a trap and absorption bottle containing water. The mixture is then heated in a water or oil bath to 65–70°, at which temperature the reaction commences and hydrobromic acid is given off smoothly. After five to six hours, the bromine has all reacted (Note 3). Towards the end of the reaction, the temperature is allowed to rise to about 100°. The contents of the flask are now distilled under diminished pressure (Note 4). The fraction boiling at 132–140°/15 mm. is collected and amounts to 280–298 g. (81–89 per cent of the theoretical amount).

2. Notes

1. The reagents must be dry or the yield will be lowered.

2. A flask fitted with a ground-glass connection to the reflux condenser will assist in reducing the amount of tar.

3. For larger runs, a longer time is required. A run of 2 kg. of caproic acid requires about fifteen hours.

4. It is best to distil the first low-boiling fractions with a water pump, since a considerable amount of hydrogen bromide is evolved. In order to obtain a light-colored product, the distillation should take place under as low pressure as possible. The α-bromo-*n*-caproic acid boils at 116–125°/8 mm. The product obtained is sufficiently pure for most purposes; upon redistillation, however, it comes over almost entirely between 128–131°/10 mm.

3. Other Methods of Preparation

α-Bromo-*n*-caproic acid has been prepared by heating *n*-caproic acid with bromine in a sealed tube to 140° [1] and with bromine and phosphorus; [2] also by the action of heat on α-bromobutylmalonic acid.[3]

[1] Z. Chem. **1868**, 616; J. prakt. Chem. (2) **1**, 7 (1870).
[2] Ber. **24**, 2222 (1891); **33**, 2381 (1900); Z. physiol. Chem. **86**, 455 (1913).
[3] J. Am. Chem. Soc. **42**, 319 (1920).

V

n-BUTYLMALONIC ESTER (ETHYL)

$$C_4H_9Br + CH_2(CO_2C_2H_5)_2 + C_2H_5ONa \rightarrow C_4H_9CH(CO_2C_2H_5)_2 + NaBr + C_2H_5OH$$

Prepared by Roger Adams and R. M. Kamm.
Checked by F. C. Whitmore and Milton Puterbaugh.

1. Procedure

A 5-l. round-bottom flask, fitted with a rubber stopper holding a reflux condenser, a separatory funnel, and a mechanical stirrer, is clamped over a steam or water bath. In the flask is placed 2.5 l. of absolute alcohol (Note 1) and then there is added gradually, through the condenser, 115 g. of clean sodium cut into pieces of suitable size. If the action becomes too violent, the mixture may be cooled by water poured over the outside of the flask. The sodium alcoholate solution is stirred, and cooled to about 50°, after which 825 g. (780 cc.) of diethyl malonate (Note 2) is added slowly through the separatory funnel. To the clear solution is added gradually 685 g. (545 cc.) of *n*-butyl bromide (Note 3). The reaction commences almost immediately and considerable heat is generated. If the addition is too rapid, the reaction may become violent enough to require cooling of the flask by pouring water over it. Up to this point, the time required is about two hours.

The reaction mixture is refluxed until neutral to moist litmus; this requires about two hours. The flask is then connected with a condenser set for distillation. As much alcohol as possible is distilled off by means of the steam or water bath.

A period of about six hours is required for this distillation and about 2 l. of alcohol is recovered.

The residue from which no more alcohol can be distilled is treated with about 2 l. of water and shaken thoroughly. The upper layer of *n*-butylmalonic ester is separated (Note 4) and distilled under diminished pressure from a 2- or a 3-l. Claisen flask. First a low-boiling portion is collected, consisting of alcohol, water, and butyl bromide; then a small intermediate fraction of unchanged malonic ester comes over; and finally *n*-butylmalonic ester boiling at 140–145°/40 mm., 130–135°/20 mm., and 235–240°/760 mm. The first fractions amount to less than 100 cc., while the main fraction amounts to 860–970 g. (80–90 per cent of the theoretical amount).

2. Notes

1. The quality of the absolute alcohol used has a very marked effect upon the yield. It is a wise procedure to reflux ordinary "absolute" alcohol with about one-twentieth of its weight of sodium and then to distil it directly into the flask in which it is to be used.

A trial run with alcohol of 98.4 per cent purity gave only a 66 per cent yield.

2. The malonic ester used should be redistilled, preferably under diminished pressure, and a 2-degree fraction used in the preparation. Ordinary commercial malonic ester contains up to 15 per cent of low-boiling impurities.

3. Redistilled *n*-butyl bromide boiling over a 1-degree range should be used.

4. It is not practical to filter off the sodium bromide either before or after the distillation of the alcohol, as the separation of the ester from the water layer is then very difficult.

3. Other Methods of Preparation

n-Butylmalonic ester has been prepared only by the action of *n*-butyl halides on sodium malonic ester.[1]

[1] Ber. **28**, 2622 (1895); J. Am. Chem. Soc. **42**, 316 (1920).

VI

o-CHLOROMERCURIPHENOL

$$C_6H_5OH + Hg(OCOCH_3)_2 \rightarrow CH_3CO_2H + HOC_6H_4HgOCOCH_3$$

$$HOC_6H_4HgOCOCH_3 + NaCl \rightarrow CH_3CO_2Na + HOC_6H_4HgCl$$

Prepared by F. C. Whitmore and E. R. Hanson.
Checked by J. B. Conant and R. M. Granara.

1. Procedure

Two liters of water is heated to boiling in a 3-l. flask. Meanwhile 50 g. of phenol, in a 250-cc. tall beaker provided with a small glass mechanical stirrer, is heated to 170° on an electric heater (Note 1). The heat is then turned off and 100 g. of powdered mercuric acetate is added gradually (five to ten minutes) to the stirred phenol. After all of the mercuric acetate has dissolved in the phenol, the mercuration mixture is poured slowly into the hot water, the burner having previously been removed (Note 2). The beaker is rinsed out with some of the hot water. The mixture is boiled for five minutes and then filtered through filter paper in a large Büchner funnel which has been previously heated by blowing steam through it. The pink residue (Note 3) consists of a small amount of dimercurated phenol and some polymerization products.

The filtrate is again brought to boiling in a clean flask and treated with a solution of 20 g. of sodium chloride in 200 cc. of boiling water. The precipitate formed is *p*-chloromercuriphenol together with some colored impurities (Note 4). The mixture is heated to boiling and filtered through a large preheated Büchner funnel. The filtrate on cooling deposits white feathery crystals of *o*-chloromercuriphenol. The mixture is

allowed to stand at least twelve hours and then filtered. The crystals are air-dried. They should be colorless and should melt above 147° (m.p. of pure substance 152°). If the product is pink or melts low it should be recrystallized from hot water. The average yield of fifteen experiments was 45 g. of ortho compound melting above 147°, which corresponds to 44 per cent of the theoretical amount.

2. Notes

1. Mercuration at lower temperatures than that recommended gives a poorer yield of the ortho compound.

2. If the heat is not removed from under the water before the mercurated phenol is added, the mixture is likely to froth over.

3. Long heating of the mercuration mixture increases the amount of pink by-product.

4. The yield of impure para compound obtained as a by-product varies from 10 to 30 g.

5. A saturated solution of bromine in glycerol should be kept at hand as an antidote for phenol burns. If all undissolved bromine is allowed to settle out before the solution is used, there is no danger of bromine burns.

3. Other Methods of Preparation

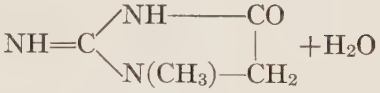
Phenol has been mercurated in water solution [1] and without the use of any solvent but the phenol itself.[2]

[1] Ber. **35**, 2855 (1902).
[2] J. Am. Chem. Soc. **43**, 622 (1921).

VII

CREATININE

$$NH{=}C(NH_2)N(CH_3)CH_2CO_2H \rightarrow$$



Prepared by Graham Edgar and W. S. Hinegardner.
Checked by H. T. Clarke and Ross Phillips.

1. Procedure

A. *Creatinine.* A mixture of 900 g. of commercial creatine hydrate (Note 1) with 550 cc. of concentrated hydrochloric acid (sp. gr. 1.19) and 150 cc. of water is warmed in a 3-l. flask on the steam bath for twenty-four hours. The hot solution is filtered and chilled to 0–5° in an ice bath, and to it is added 1000 cc. of 28 per cent aqueous ammonia (sp. gr. 0.90). The flask is immersed in an ice-salt bath and the mixture is stirred vigorously until the temperature falls to 0°, when the crystalline creatinine is filtered off, washed with ice-cold 28 per cent aqueous ammonia (Note 2) until the filtrate is free of chlorides, and finally with ice-cold methyl alcohol; the product (Note 3) is then dried to constant weight at 40–50°. The yield (Note 4) is 545–555 g. (80–81 per cent of the theoretical amount).

B. *Creatinine Zinc Chloride.* An intimate mixture of 400 g. of commercial creatine hydrate and 400 g. of fused zinc chloride is heated in a porcelain dish over a small flame. The mixture melts to a viscous liquid which soon solidifies. The flame is removed when the mixture can no longer be stirred. The mass, when cold, is broken up, and stirred with 500 cc. of cold water until the lumps are softened; the crude creatinine zinc chloride is filtered off with suction, by the use of a hardened filter paper,

and washed with ice water to remove excess zinc chloride. The crude material is now dissolved in 6 l. of boiling 25 per cent aqueous acetic acid, filtered with the use of a little decolorizing carbon, and the solution allowed to stand for forty-eight hours. The crystals that have separated are filtered off, washed with ice water, and dried. Weight 220–230 g. The filtrate and washings are evaporated to 4.5 l. under reduced pressure in a 12-l. flask; 6.5 l. of methyl alcohol is added and the mixture allowed to stand in a cool place for twenty-four hours. The crystals that separate are filtered off, washed with cold water and dried, and an additional 150–160 g. is thus obtained. The total yield is 370–380 g. (76–78 per cent of the theoretical amount).

C. *Creatinine Picrate.* A mixture of 300 g. of commercial creatine hydrate with 190 cc. of concentrated hydrochloric acid (sp. gr. 1.19) and 50 cc. of water is warmed in a glass or porcelain dish on a steam bath for twenty-four hours. The resulting mass of creatinine hydrochloride crystals is dissolved in 1 l. of water, boiled with a little decolorizing carbon, and filtered. The solution is then diluted to 4 l. with distilled water, and heated to boiling in a 12-l. flask under a reflux condenser. To the hot solution is added, with good stirring, a solution of 500 g. of technical picric acid (containing 10 per cent of water) in 1250 cc. of warm methyl alcohol. Stirring is continued for one hour on the steam bath and the solution allowed to cool. The crystalline precipitate of creatinine picrate is filtered off, washed well with cold water, and dried. It forms long needles which melt at 220°; the melting point (Note 5) is unchanged on recrystallization from hot water. The yield is 620–630 g. (89–90 per cent of the theoretical amount).

2. Notes

1. As a rule, the commercial product, which contains one mol of water of crystallization, is entirely satisfactory; but if it is dark in color, it may be recrystallized from water with the use of decolorizing carbon.

2. Creatinine dissolves readily in pure water but is only slightly soluble in cold concentrated ammonia, while ammonium chloride is freely soluble.

3. The creatinine so prepared is practically 100 per cent pure; its recrystallization, while not recommended, may be carried out by dissolving, as rapidly as possible, 1 part by weight in 5 parts of water previously warmed to 65°, and then immediately adding to the warm solution double its volume of acetone, chilling in ice, and filtering after a few hours. The product is finally washed with acetone and dried. About one-third is lost in the filtrate.

4. The yield could be slightly increased by so modifying the conditions that the total volume of filtrate would be smaller, but this would involve an undue amount of trouble.

5. Special attention was given to the melting point determination, since two values, 205° and 212–213°, have been recorded in the literature.

3. Other Methods of Preparation

Creatinine has been prepared generally from urine [1] or muscle,[2] though its formation from creatine by the action of mineral acids has also been studied.[3] The conversion of creatine into creatinine has also been effected by heating in an autoclave [4] and by treatment with zinc chloride.[5] The above technique has been developed [6] since creatine has become available in relatively large quantities as a by-product.[7]

[1] Ann. **119**, 39 (1861); **159**, 279 (1871).
[2] Gazz. chim. ital. **17**, 382 (1887).
[3] Ann. **62**, 298 (1847); J. Am. Chem. Soc. **45**, 2242 (1923).
[4] J. Biol. Chem. **8**, 399 (1910).
[5] Jahresb. **1857**, 544; J. Biol. Chem. **18**, 183 (1914).
[6] J. Biol. Chem. **56**, 3, 881 (1923).
[7] J. Ind. Eng. Chem. **14**, 984 (1922).

VIII

CUPFERRON

$$C_6H_5NHOH + C_4H_9ONO + NH_3 \rightarrow C_6H_5N(NO)ONH_4 + C_4H_9OH$$

Prepared by C. S. Marvel.
Checked by Oliver Kamm.

1. Procedure

The moist phenylhydroxylamine obtained from 1000 g. of nitrobenzene, by the method described on page 57, is weighed and dissolved in 4.5 l. of ordinary ether (Note 1). The ether-insoluble material (sodium chloride and water) is also weighed, the difference between the two weighings being a fairly accurate measure of the amount of phenylhydroxylamine in solution.

The ether solution is filtered through a dry filter paper into a 5-l. round-bottom flask which is fitted with an efficient mechanical stirrer and immersed in an ice-salt bath. When the temperature of the solution has fallen to 0° (Note 2), a rapid stream of dry ammonia gas, from a cylinder of compressed gas, is passed into the solution.

After about fifteen minutes, the theoretical amount of freshly distilled *n*-butyl nitrite (95 g. for every 100 g. of phenylhydroxylamine) is added slowly through a dropping funnel (Note 3). The addition of butyl nitrite usually requires about one hour (Note 4), during which time the stream of ammonia gas is continued in order that ammonia may always be in excess. If this precaution be not observed, a colored product will result. The temperature of the reaction mixture should be maintained below 10° and this may be done best by controlling the rate at which the butyl nitrite is added. An appreciable rise in tem-

perature will cause the volatilization of considerable quantities of ether and of ammonia (Note 5).

After the butyl nitrite has been added, the reaction mixture is stirred for about ten minutes longer in order to insure completion of the reaction, after which the cupferron is filtered off and washed several times with small portions of fresh ether. The product is spread on sheets of paper until all traces of ether have been lost, and is then stored in bottles where it is exposed to the vapors of ammonium carbonate. This may be done by protecting each cork with a double sheet of filter paper and placing a lump of ammonium carbonate between the cork and the filter paper.

The yield of cupferron from a given weight of phenylhydroxylamine averages 85–90 per cent of the theoretical amount.

2. Notes

1. The solvent ether may be replaced by benzene, but this modification offers no advantages for the preparation of cupferron on a laboratory scale.

2. The temperature must be kept low. If it is not, the material is generally colored brown and the reaction does not run smoothly. Probably the most important factor in securing successful results is always to have an excess of ammonia present.

3. The butyl nitrite is freshly distilled as a general precaution, because a product which has stood for some time is often partially decomposed.

4. In the preparation of cupferron, it has been recommended that the butyl nitrite be added all at one time. This procedure is satisfactory only when the amount of phenylhydroxylamine used is less than 200 g.; otherwise the reaction becomes extremely vigorous and an excessive proportion of ether is lost. The directions given above, on the other hand, are adaptable for the preparation of large quantities of cupferron. For the rapid preparation of small quantities of material, the butyl nitrite may be added all at one time, provided sufficient excess of ammonia is present.

5. It is found that 75 per cent of the ether and 95 per cent of the butyl alcohol used may be recovered, and that one man, working six to seven hours, is able to prepare 800 g. of cupferron. The recovered ether may be used over again, provided the following procedure is followed: The phenylhydroxylamine is dissolved in a little fresh ether, the solution cooled and treated with ammonia, then the recovered ether added. This precaution is necessary owing to the presence of some butyl nitrite in the recovered ether.

3. Other Methods of Preparation

Nitroso-β-phenylhydroxylamine, of which cupferron is the ammonium salt, has been made by the action of sodium nitrite and hydrochloric acid on β-phenylhydroxylamine,[1] of hydrogen peroxide on normal phenyldiazotates,[2] of sodium alcoholate and hydroxylamine on nitrobenzene,[3] of nitric oxide on phenyl magnesium bromide,[4] and by the action of permonosulfuric acid on aniline in the presence of amyl nitrite.[5]

Cupferron has usually been prepared from a mixture of alkyl nitrite and β-phenylhydroxylamine in the presence of ammonia in ether or benzene solution,[6] but it has also been made by the zinc dust reduction of nitrobenzene in the presence of amyl nitrite and ammonium hydroxide solution.[7]

[1] Ber. **27**, 1435, 1554 (1894); **52**B, 1839 (1919); J. Am. Chem. Soc. **41**, 280 (1919).
[2] Ber. **42**, 3575 (1909).
[3] Ber. **29**, 1885 (1896).
[4] Ann. **329**, 191 (1903).
[5] D. R. P. 227,659; Frdl. **10**, 126 (1910).
[6] Chem. Z. **35**, 913 (1911); J. Ind. Eng. Chem. **3**, 629 (1911); **12**, 799 (1920); J. Am. Chem. Soc. **41**, 280 (1919).
[7] D. R. P. 227,659; Frdl. **10**, 126 (1910).

IX

DI-*p*-TOLYLETHANE (*unsym.*)

$$2C_6H_5CH_3 + CH{\equiv}CH(HgSO_4) \rightarrow (CH_3C_6H_4)_2CHCH_3$$

Prepared by J. S. Reichert and J. A. Nieuwland.
Checked by Oliver Kamm.

1. Procedure

A 2-l. flask, containing 700 cc. of toluene, 70 cc. of concentrated sulfuric acid, and 7 g. of mercuric sulfate, is fitted with a stirrer, a thermometer reaching into the liquid, and an inlet tube connected with a gasometer containing acetylene, as shown in Fig. 1 (Note 1). The flask and its contents are tared and cooled to 10° before the absorption of acetylene is begun. The gas from the tank, *A*, is washed free from acetone by being passed first through water in the gasometer, *B*, and then through the concentrated sulfuric acid wash bottle, *C*.

The acetylene is absorbed rapidly, with the evolution of considerable heat. The temperature of the reaction mixture is maintained at 10–15° by immersing the flask in a freezing mixture. When at intervals the reaction slows down, it becomes necessary to sweep the system free from air which accumulates in the flask. The absorption is continued until about 60 g. of acetylene has been absorbed, which requires a period of about two hours (Note 2). During the absorption, the mixture turns first a reddish brown, then a dark brown, and finally almost black.

The reaction mixture is freed from the acid by washing once with pure water and then with sodium carbonate solution, to which some sodium chloride is added to aid the separation of

the hydrocarbon layer. If emulsification takes place, the addition of ether will remedy the difficulty.

The toluene layer is transferred to a 1-l. flask, without drying, and the unchanged toluene distilled off; the ditolylethane is then collected over a range of 295–310°. There is practically no intermediate fraction, but a tarry residue of about 75 g. remains in the flask. Upon redistillation, the ditolylethane is

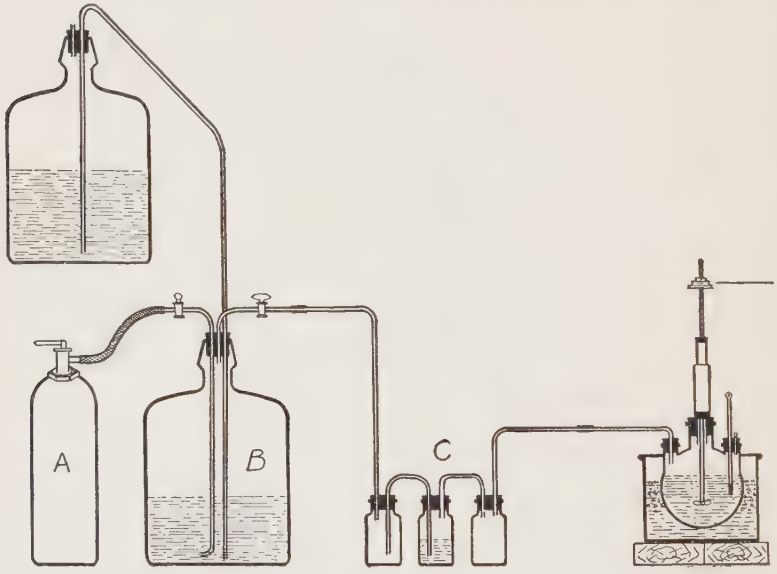


FIG. 1.

collected at 295–300°. The yield is 290–310 g. (60–64 per cent of the theoretical amount) (Note 3).

2. Notes

1. The acetylene is absorbed with unexpected rapidity so that it is unnecessary to deliver the gas beneath the surface of the liquid. In an ordinary reaction involving a gas it would be advisable to use a special stirrer of the type illustrated in Org. Syn. **3,** p. 29, and to deliver the gas beneath the distributing tube of the stirrer.

2. It is scarcely necessary to remove the flask for weighing until near the end of the experiment, since the volume of acetylene is known and practically complete absorption takes place. If a tank of compressed gas is not available, the acetylene may be prepared from calcium carbide by the usual laboratory methods.[1]

3. Subsequent redistillation yields a product boiling practically over a 2-degree range. The best product was obtained by a final fractionation under diminished pressure, when the boiling point was found to be 144–145°/8 mm.

4. Xylene, mesitylene, ethylbenzene, and benzene condense with acetylene in a manner similar to that described above for toluene, although the yields are usually lower.[2]

3. Other Methods of Preparation

Ditolylethane has been obtained also from the reaction between paraldehyde and toluene in the presence of sulfuric acid,[3] from the reaction between ethylidene chloride and toluene in the presence of aluminium chloride,[4] and by heating α-ditolylpropionic acid in the presence of lime.[5]

[1] Cf. C. A. **3**, 2887 (1909).
[2] J. Am. Chem. Soc. **45**, 3090 (1923)
[3] Ber. **7**, 1193 (1874).
[4] Ann. **235**, 313 (1886).
[5] Ber. **15**, 1476 (1882)

X

ETHYL OXOMALONATE

$$CH_2(CO_2C_2H_5)_2 + 2N_2O_3 \rightarrow CO(CO_2C_2H_5)_2 + H_2O + 4NO$$

Prepared by A. W. Dox.
Checked by C. S. Marvel and R. L. Shriner.

1. Procedure

Into a 500-cc. Erlenmeyer flask containing 200 g. of ethyl malonate, and cooled to 0° by surrounding with cracked ice and salt, a rapid current of nitrous anhydride is passed. The gas is generated by dropping concentrated nitric acid through a separatory funnel upon dry arsenious oxide contained in a 500-cc. Florence flask placed upon a tripod and wire gauze. The arsenious oxide should be in lumps about the size of a pea. An empty flask is inserted between the generator and the absorption flask and the gas dried by passage through a calcium chloride tube (Note 1). As the evolution of gas slows down, gentle heat may be applied with a burner. The ethyl malonate becomes dark green in color. There should be an increase in weight of about 200 g. in two to three hours.

The liquid is left in the freezing mixture for several hours, then gradually allowed to come to room temperature (Note 2). Red gases are slowly evolved. After standing for two days or more at room temperature, the liquid is transferred to a distilling flask provided with a capillary air intake, and the delivery tube connected with a water-cooled condenser and receiver. The distillation is performed under diminished pressure, by the use of a water pump. Considerable nitric oxide is evolved before the pressure drops to about 70 mm. (Note 3).

The first fraction consists mainly of water, a little ethyl acetate, and some ethyl oxomalonate which recombines with the water to form ethyl mesoxalate. When the pressure has dropped to 45 mm. and the temperature has risen to 110°, the receiver is

changed (Note 4). The main product, ethyl oxomalonate, now distils at 110–135°/45–50 mm. If the oxidation has been complete, very little residue is left (Note 5). Redistillation gives a golden-yellow liquid boiling between 103–108°/15 mm. The yield is 160–165 g. (74–76 per cent of the theoretical amount).

2. Notes

1. The yield of ethyl oxomalonate is decreased if the nitrous anhydride is not dried.

2. If the temperature is raised too rapidly, the liberation of gases causes the mixture to boil too vigorously.

3. A motor pump is not recommended because the nitric oxide is apt to cause corrosion. If too high a vacuum is used at first, a residue of ethyl iso-nitrosomalonate may remain.

4. The remainder of the distillation must be conducted with extreme care. As soon as the ethyl oxomalonate has partly distilled over and the temperature has risen somewhat, the remaining iso-nitroso compound begins to decompose and sometimes liberates gases so rapidly that the thermometer and capillary tube may be blown out of the flask. If the manometer is watched closely, and at the first sign of liberation of gas, as evinced by a sudden increase in pressure, a wet towel is placed around the flask, the reaction can be slowed down.

5. In case any considerable amount of residue remains above 135° at 45 mm., it is heated at ordinary pressure to a higher temperature until no more nitric oxide is given off, then distilled as before.

3. Other Methods of Preparation

Ethyl oxomalonate is obtained from a variety of intermediates [1] but the only method which appears of practical value consists in the oxidation of ethyl malonate by means of oxides of nitrogen. This reaction, carried out in two steps by Bouveault and Wahl,[2] was studied by Schmidt [3] and subsequently considerably improved by Curtiss [4] and also by Meyer.[5]

[1] Beilstein, **3**, 769–770 (Fourth Edition). [2] Compt. rend. **137**, 196 (1903).
[3] Compt. rend. **140**, 1400 (1905). [4] Am. Chem. J. **33**, 603 (1905); **35**, 477 (1906).
[5] Bull. soc. chim. (4) **9**, 423 (1911); C. A. **5**, 3229 (1911).

XI

ETHYL PROPANE-1,1,2,3-TETRACARBOXYLATE

$$CH_2(CO_2C_2H_5)_2 + CH(CO_2C_2H_5)=CHCO_2C_2H_5 + (C_2H_5ONa) \rightarrow CH(CO_2C_2H_5)_2CH(CO_2C_2H_5)CH_2CO_2C_2H_5$$

Prepared by H. T. Clarke and T. F. Murray.
Checked by C. S. Marvel and M. M. Brubaker.

1. Procedure

In a 5-l. flask, fitted with a stirrer, reflux condenser, and dropping funnel, is placed 1000 g. of absolute ethyl alcohol; 92 g. of sodium, cut into strips, is then added through the condenser at such a rate that the alcohol does not boil too vigorously. When all the sodium is in solution, the flask is cooled and 800 g. of ethyl malonate added through the condenser, with stirring. The mixture is warmed gently on the steam bath and 700 g. of ethyl fumarate (Note 1) added from the dropping funnel. During this addition the solution is kept boiling gently, heat being applied if necessary (Note 2). The mixture is boiled for one hour after the ethyl fumarate has been added. It is then cooled and 250 g. of glacial acetic acid is added.

Most of the alcohol is distilled off under slightly reduced pressure on the steam bath and the residue is poured into sufficient distilled water to dissolve all the solid. The water layer is separated and extracted four times with carbon tetrachloride, which is added to the ester layer. The ester-carbon tetrachloride mixture is washed twice with water and the water washings extracted once with carbon tetrachloride. The carbon tetrachloride is distilled off under atmospheric pressure through a column, the moisture being carried over simultaneously.

The residue is then distilled under reduced pressure, when the ethyl propane-1,1,2,3-tetracarboxylate comes over at 182–184°/8 mm. The yield is 1261–1273 g. (95–96 per cent of the theoretical amount).

2. Notes

1. The ethyl malonate and ethyl fumarate should be redistilled under reduced pressure, and the material boiling over a 2-degree range should be collected.

2. Heat is developed during the reaction, and the mixture may be kept boiling by adding the ethyl fumarate at a suitable rate.

3. Other Methods of Preparation

Now that fumaric and maleic acid are available commercially, the most convenient method of preparing the above ester consists in condensing ethyl malonate with ethyl fumarate[1] or ethyl maleate.[2] It has also been prepared by condensing malonic ester with ethyl chlorosuccinate[3] and with ethyl ethoxysuccinate.[4]

[1] Ber. **24**, 2889 (1891); J. prakt. Chem. (2) **45**, 56 (1892); J. Chem. Soc. **73**, 1007 (1898); Ann. **341**, 102 (1905).

[2] J. prakt. Chem. (2) **45**, 56 (1892).

[3] Ber. **23**, 3759 (1890).

[4] Chem. Zentr. **1903** (II), 943; Ann. **341**, 104 (1905).

XII

GLYCINE

$$CH_2{=}NCH_2CN + 3H_2O + 2HBr \rightarrow CH_2O + HBr \cdot NH_2CH_2CO_2H + NH_4Br$$

$$HBr \cdot NH_2CH_2CO_2H + C_5H_5N \rightarrow NH_2CH_2CO_2H + C_5H_5N \cdot HBr$$

Prepared by H. T. Clarke and E. R. Taylor.
Checked by Roger Adams and W. F. Tuley.

1. Procedure

In a 5-l. flask fitted with a downward condenser, are placed 340 g. of methylene aminoacetonitrile (p. 47) and 2500 g. of 48 per cent hydrobromic acid (Note 1). The mixture is heated on the steam bath for three hours (Note 2). The pressure in the apparatus is then reduced and dilute acid and formaldehyde are distilled into a water-cooled receiver until the separation of ammonium bromide from the reaction mixture causes bumping. This occurs when approximately half of the liquid has been distilled over. The ammonium bromide is filtered from the hot liquid and washed with a small amount of cold water; the filtrates are returned to the flask and distillation continued as nearly as possible to dryness (Note 3). The residue is dissolved in 2 l. of cold methyl alcohol and filtered; to the filtrate is added 350 cc. of pyridine, with vigorous shaking (Note 4).

The mixture is allowed to stand over night and the precipitated glycine filtered off and washed with methyl alcohol (Note 5) until the washings are free from bromides. The product is dissolved in 300 cc. of boiling distilled water and the solution filtered with the use of a little decolorizing carbon; the filtrate is allowed to cool to 40–50°, when 1500 cc. of methyl alcohol is added with hand stirring. If the product is colored, the procedure, just described, of dissolving in water and reprecipitating with methyl alcohol is repeated. The glycine that

separates is filtered off when the mixture is cold and washed with methyl alcohol until a sample (Note 6) is found to be free from ammonia on testing with Nessler solution (Note 7). If a second precipitation is made, the glycine is practically free from ammonium salts and washing with methyl alcohol is unnecessary. Not more than 1 l. of methyl alcohol should be necessary for this purpose; if positive tests continue to be obtained, an ammonia-free product may be secured by treating the aqueous solution for a short time with a water-softening zeolite, filtering and crystallizing or precipitating with alcohol.

The yield is 115–140 g. (31–37 per cent of the theoretical amount) of a colorless product which melts with decomposition at 225–230° (Note 8).

The distillate from the reaction mixture may be redistilled under atmospheric pressure with the use of a column; the fraction boiling at 125–126° may be collected, when one-third to one-half the amount of hydrobromic acid originally taken can be recovered. The foreruns contain formaldehyde.

2. Notes

1. If preferred, 3000 g. of 40 per cent acid may be taken. Hydrobromic acid is employed in preference to other mineral acids on account of the high solubility of ammonium bromide in methyl alcohol.

2. Hydrolysis takes place readily, with a slight evolution of heat, so that actual boiling over a free flame is unnecessary.

3. The residue consists of a syrup (largely glycine hydrobromide) mixed with crystals of ammonium bromide. It has a strong odor of formaldehyde.

4. A technical grade of pyridine may be employed if this is colorless and distils not lower than 100° nor higher than 140°.

5. Ammonium bromide dissolves in about eight times its weight of methyl alcohol. It is much less soluble in absolute ethyl alcohol, requiring about 30 parts of that solvent.

6. The sample should be taken from the lower part of the cake on the funnel by means of a glass tube, since the upper layers become free of impurities first.

7. The sample of glycine must be dry before testing, as traces of impurities generally present in the methyl alcohol give a precipitate with Nessler solution. To carry out the test, 0.1–0.2 g. of dry product is dissolved in 3 to 5 cc. of distilled water containing a few drops of sodium hydroxide solution, and 1 cc. of Nessler solution is added.

8. A further small quantity of impure glycine can be isolated by concentrating the filtrates obtained on recrystallization. The liquors from the first precipitation, containing ammonium bromide, pyridine hydrobromide, excess pyridine, and alcohol-soluble by-products, may be treated as follows: The mixture is first acidified with mineral acid and the methyl alcohol recovered by distillation with a column. The residue is rendered strongly alkaline and the bulk of the ammonia removed by boiling under a reflux condenser; wet pyridine can be recovered by downward distillation and treatment of the distillate with solid sodium hydroxide.

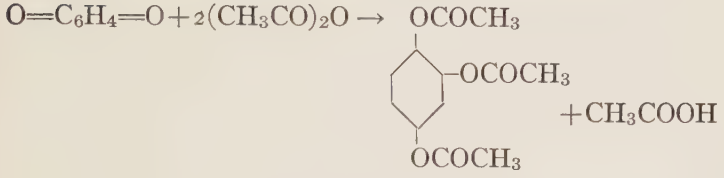
3. Other Methods of Preparation

Glycine hydrochloride has been prepared by the action of hydrochloric acid upon hippuric acid,[1] upon aminoacetonitrile,[2] upon methylene aminoacetonitrile,[3] and upon ethyl phthaliminoacetate;[4] its conversion into free glycine by methods involving silver or lead oxides is apt to be troublesome. The classical method of preparing glycine by the interaction of chloroacetic acid and ammonia[5] is unsatisfactory, owing to the laborious process of isolation through the copper salt, which, moreover, rarely gives a product entirely free of ammonia. The hydrolysis of methylene aminoacetonitrile by successive treatments with barium hydroxide and sulfuric acid[6] furnishes a more satisfactory method, but the final product is seldom entirely pure, partly owing to the difficulty in obtaining pure barium hydroxide. The same objection applies to the hydrolysis of aminoacetonitrile by means of barium hydroxide.[7]

[1] J. prakt. Chem. (2) **37**, 157 (1888).
[2] Ann. **278**, 236 (1894).
[3] Ber. **27**, 60 (1894).
[4] Ber. **22**, 428 (1889).
[5] Ann. **266**, 295 (1891).
[6] Biochem. J. **16**, 702 (1922).
[7] Ann. **278**, 237 (1894).

XIII

HYDROXYHYDROQUINONE TRIACETATE



Prepared by E. B. Vliet.
Checked by Roger Adams and H. O. Calvery.

1. Procedure

Twelve grams of concentrated sulfuric acid is added to 180 g. of acetic anhydride in a 600-cc. beaker, after which 60 g. of benzoquinone (Note 1) is added gradually in small portions with constant mechanical stirring. The temperature rises and should be held at 40–50° during the addition of the quinone. A temperature higher than 50° leads to decomposition of the product while a temperature lower than 40° causes a much slower reaction. Good temperature control can be obtained by using care in adding the quinone and by the use of a cooling bath and efficient stirring. The reaction goes smoothly and does not evolve an excessive amount of heat.

After all the quinone has been added, the solution is allowed to stand. It should be watched closely at first to see that the temperature does not rise above 50°, but at the same time it is well not to cool it below 40°. When the mixture starts to cool of its own accord, a precipitate begins to form. As soon as the mixture has cooled to about 25° (Note 2), it is poured into 750 cc. of cold water, whereupon a white precipitate separates. This is cooled to about 10° and filtered off with suction. The

product is recrystallized from 250 cc. of 95 per cent ethyl aclohol and dried. The drying is best done in a vacuum desiccator, through which a very small stream of air is allowed to sweep. Calcium chloride is the best drying agent.

The product is practically white and rather granular; it melts at 96–97°. The yield is 120–123 g. (85–87 per cent of the theoretical amount). The product is fairly reactive and tends to decompose upon standing (Note 3), especially if care be not used in drying and handling. If it is to be used as a starting material for other syntheses, it is advisable to use it as soon as possible.

2. Notes

1. The quality of the product depends to a large extent upon the purity of the benzoquinone; if the latter is dark, it is advisable to crystallize it from benzene before using it. (See Org. Syn. **2**, 86.)

2. It is quite desirable to have the reaction mixture cooled to about 25° before it is added to the water. If it is warm when added to the water, an oil will separate which solidifies slowly in the form of lumps.

3. The hydroxyhydroquinone triacetate keeps quite satisfactorily in an atmosphere of carbon dioxide.

3. Other Methods of Preparation

The method described above is essentially the same as that of Thiele,[1] which has been patented by F. Bayer and Company.[2] Hydroxyhydroquinone triacetate has also been obtained by acetylating hydroxyhydroquinone formed by the alkali fusion of hydroquinone.[3]

[1] Ber. **31**, 1247 (1898); Gazz. chim. ital. **40** (2) 349 (1910).
[2] D. R. P. 101,607 and 107,508; Frdl. **5**, 155–6 (1898).
[3] Monatsh. **5**, 590 (1884).

XIV

o-IODOPHENOL

$$2HOC_6H_4HgCl + 2I_2 \rightarrow HgI_2 + HgCl_2 + 2IC_6H_4OH$$

Prepared by F. C. Whitmore and E. R. Hanson.
Checked by J. B. Conant and R. M. Granara.

1. Procedure

A 2-l. round-bottom short-neck flask is equipped with a glass mechanical stirrer. A suspension of 165 g. of *o*-chloromercuriphenol (p. 13) (m.p. 147° or higher) in 500 cc. of chloroform is placed in the flask and treated with 127 g. of iodine, the stirring being continued until a small sample on filtration shows no unreacted iodine. This requires from one to two hours. The solid inorganic mercury compounds are removed by suction filtration. The filtrate is distilled from a 1-l. distilling flask on the water bath to remove most of the chloroform, which is saved for later runs (Note 1). The residual liquid is shaken vigorously with a solution of 5 g. of potassium iodide in 10 cc. of water, to remove dissolved mercuric iodide. The heavier layer, which still possesses a reddish color, is transferred without drying to a 200-cc. Claisen flask and distilled under diminished pressure. At first a small amount of chloroform and water distils over, after which the higher-boiling material is collected in a separate receiver. Small amounts of inorganic mercury compounds remain in the flask (Note 2).

The *o*-iodophenol solidifies upon cooling. The yield of material melting at 32–34° is 70 g. (63 per cent of the theoretical amount). The product obtained in this way is slightly yellow. If a purer product is desired, it may be redistilled *in vacuo*.

Most of the crude material will distil over a 5-degree range (b.p. 130°/18 mm. and 186°/160 mm., m.p. 43°).

2. Notes

1. About 460 cc. of chloroform can be recovered, the time required being one hour.

2. The first distillation of the iodophenol should be carried out under a good vacuum, 40 mm. or lower. The redistillation may be conducted at a higher pressure if desired.

3. Since the iodophenol has a most persistent odor, care should be exercised in working with it. A solution of bromine in glycerol may be used as an antidote for burns from the iodophenol (p. 14).

3. Other Methods of Preparation

o-Iodophenol has been made by diazotization from *o*-aminophenol [1] and from *o*-iodoaniline.[2] It has been obtained by heating *o*-iodosalicylic acid.[3] Mixed with its para isomer and diiodophenol, it has been made by treating a dilute phenol solution with iodine and iodic acid,[4] and it has also been obtained from an alkaline solution of phenol and iodine in the presence of mercuric oxide,[5] and from dry sodium phenolate and iodine in carbon disulfide.[6]

[1] Ber. **8**, 820 (1875); Ann. **241**, 68 (1887).
[2] Chem. Zentr. **1910** (II), 304.
[3] Ann. **120**, 315 (1861).
[4] Z. Chem. **1866**, 662; **1868**, 322.
[5] Ber. **2**, 523 (1869); **6**, 1251 (1873).
[6] Ber. **16**, 1897 (1883); **20**, 3363 (1887).

XV

KETENE

$$CH_3COCH_3 \rightarrow CH_2{=}CO + CH_4$$

Prepared by C. D. Hurd.
Checked by Oliver Kamm.

1. Procedure

A. *Preparation of ketene.* The arrangement of the apparatus is shown in Fig. 2 (Note 1). The graduated separatory funnel, shown in the diagram, filled with 125 cc. of commercial acetone, leads into a 500-cc. round-bottom flask which, in turn, is connected by gas-tight joints (Note 2) to a glass combustion tube filled with broken porcelain, a spiral or bulb condenser, a two-way stopcock, and a reaction flask. In the reaction flask is placed the material with which the ketene is to react (Note 3). A second reaction flask may be placed in series, if desired, to ascertain if any ketene escaped reaction in the first flask.

Prior to either of these steps, fourteen of the twenty burners of the combustion furnace are lighted (Note 4) and tiles are placed over the lighted burners, which finally must be adjusted to yield a maximum temperature. The first two and last four burners are unused.

When the furnace is fully heated, boiling water is placed beneath the round-bottom flask and cold water passed through the condenser. Acetone is now dropped in at the rate of 3–4 cc. per minute. About half the acetone should be recovered as distillate in cylinder *B* (Note 5). Ketene, admixed with methane, carbon monoxide, and ethylene, passes into the reaction flasks (Note 6) in 25–29 per cent yields. The flow may be interrupted at will by checking the acetone flow.

B. *Preparation of acetanilide.* Since ketene is a highly reactive gas, it is usually prepared for immediate consumption instead of being isolated as such. It reacts with various groups which contain hydrogen, such as hydroxyl, amino, mercaptan, hydroxylamino, etc., forming acetyl derivatives.

Twenty-five grams of aniline is placed in the reaction flask, *D*, and 50 cc. of dry ether added as solvent (Note 7). A second reaction flask is connected at *C*, in which is placed 5 g. of aniline,

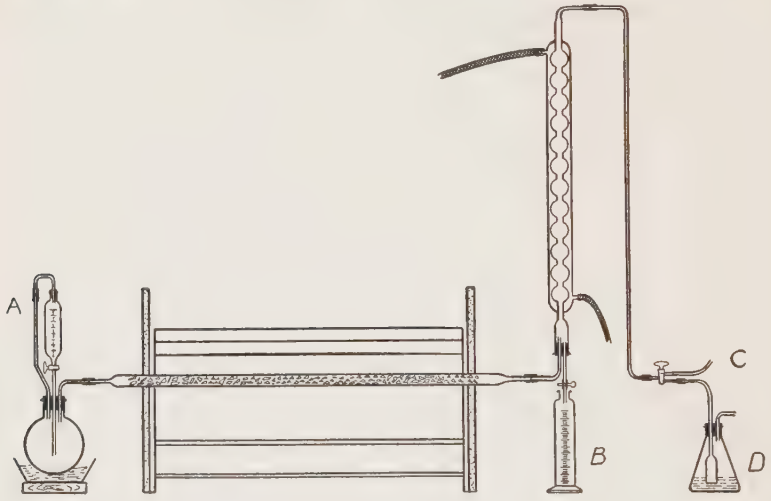


FIG. 2.

dissolved in 20 cc. of ether. This prevents the escape of ketene vapor at the beginning and at the close of the operation (Note 5). In all, 85 cc. of acetone is passed through the apparatus, 39 cc. of which is recovered as distillate. Therefore, 44 cc. (or 35 g.) of acetone is decomposed. The duration of the run is about thirty minutes. Twenty-one grams of acetanilide, which corresponds to a yield of 25.8 per cent, based upon the amount of acetone decomposed, is isolated from the reaction mixture.

2. Notes

1. *The apparatus.* A graduated dropping funnel and a graduated cylinder for the distillate are chosen because of convenience in determining the volume of decomposed acetone.

The bulb (or spiral) condenser is chosen because of its efficiency. With an ordinary condenser, it is necessary to insert two U-tubes, cooled by ice, between the condenser and the reaction flask, to remove all the acetone from the ketene. In many reactions, however, this admixed acetone will do no harm. This part of the apparatus is designed to eliminate the loss of ketene by solvent action, prior to its entry into the reaction flask.

A wide-mouth delivery tube in the reaction flask is essential to prevent clogging, when a solid product is formed. Automatic stirring in the reaction flask may be used to advantage in certain instances. There is constant agitation, of course, as the gaseous decomposition products bubble through.

Either Scotland glass or Pyrex is satisfactory for the combustion tube. An estimate of the temperature is 650° (Note 4). The life of the tube is lengthened if it rests upon a layer of thin asbestos paper. The tube is filled with pieces of broken porcelain, to serve as a " heat reservoir "; there is no catalytic effect. The porcelain blackens during the reaction.

2. *Care in assembly.* Since this is a gaseous reaction, it is essential that the apparatus be free from leaks; thus, corks are eliminated wherever possible. The ends of the combustion tube and the top of the condenser are drawn to the diameter of the connecting tubes and joined by a piece of thick-walled rubber tubing. Care should be taken to have the ends of the glass tubes come into contact. The rubber tube situated between the furnace and condenser is protected by the asbestos screen, but a further essential precaution is taken, namely, that this end of the combustion tube extend a considerable distance from the furnace.

The stoppers in the reaction flask and at the top of the dropping funnel are of rubber; the other two are well-selected corks, bored perfectly and painted both inside and out with water-glass, one day previous to being used.

3. The apparatus may be calibrated by allowing the ketene to react with 5N alkali and titrating the excess alkali with acid.

4. With an electric combustion furnace, wherein a tempera-

ture of 695–705° is maintained, consistent yields of 35–40 per cent ketene are produced. The best rate of flow in such a case is 4–6 cc. per minute, with recovery of 60–80 per cent of the original acetone as distillate. Although yields of ketene ranging above 45 per cent have been obtained frequently with this apparatus, they could not be duplicated consistently.

5. The thermal decomposition of ketene into carbon monoxide and ethylene is prevented, as far as possible, by the rapid removal of ketene from the hot tube, which is accomplished by the undecomposed acetone vapor. About half the acetone originally used should be collected unchanged as distillate by the vertical condenser. The yield of ketene will fall considerably if less distillate is formed.

6. Ketene gas is very irritant when breathed, and hence proper cautions should be taken to avoid inhalation.

7. An ice bath surrounding the reaction flask is usually employed, not only to prevent the vaporization of the solvent, but also to promote a greater solubility of ketene.

3. Other Methods of Preparation

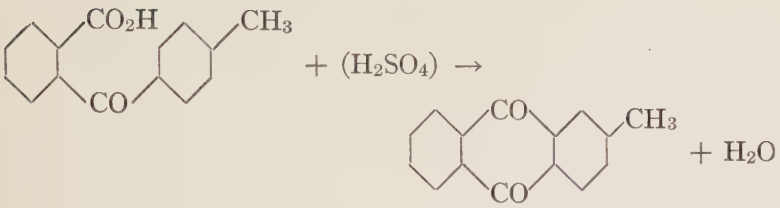
In addition to the above method, based upon the work of Schmidlin and Bergman [1] as modified by Hurd and Cochran,[2] ketene has been prepared by the pyrogenic decomposition of acetic anhydride,[3] of ethyl acetate, and of triacetin.[4] In the last instance, acrolein and acetic acid are formed simultaneously.

Ketene has also been formed by the action of zinc upon an ethereal solution of bromoacetyl bromide.[5] Carbon monoxide and diazomethane, diluted with ether, when passed through a quartz tube at 400–500°, yield ketene and nitrogen.[6]

[1] Ber. **43**, 2821 (1910).
[2] J. Am. Chem. Soc. **45**, 515 (1923).
[3] J. Chem. Soc. **91**, 1938 (1907); **97**, 1968 (1910).
[4] Ber. **47**, 2393 (1914).
[5] Ber. **41**, 594 (1908).
[6] Ber. **45**, 508 (1912).

XVI

β-METHYL ANTHRAQUINONE



Prepared by L. F. Fieser.
Checked by Roger Adams and R. L. Shriner.

1. Procedure

The *p*-toluyl-*o*-benzoic acid which is obtained from 100 g. of phthalic anhydride (p. 73), and which should weigh 157 g., is mixed with 1400 g. of fuming sulfuric acid (20 per cent anhydride) (Note 1) in a 2-l. flask protected by a calcium chloride tube; and the mixture is heated on the steam bath for two hours with occasional shaking (Note 2). The clear, deep red solution is poured when cold upon cracked ice in a 4-l. beaker. The methyl anthraquinone separates and is digested for twenty minutes by passing in steam, after which it is filtered by suction. A flannel cloth is used in the filter, or a filtros plate may be cemented into a Büchner funnel with water-glass. The precipitate is washed well with hot water, after which it is returned to the beaker and digested as before with hot water to which is added a slight excess of ammonia, beyond that required to neutralize any acid present.

The product is filtered and dried to constant weight. The filtrate will be clear and will give no precipitate with hydrochloric acid if the conditions of condensation have been correct.

The β-methyl anthraquinone is pale tan in color and weighs from 118 to 130 g. (86–95 per cent of the theoretical amount, based upon the weight of acid taken). It is practically pure, melting at 173°. Upon crystallization from alcohol in the presence of bone-black, it forms long, silken, almost colorless needles, melting constantly at 173.5° (176° cor.).

2. Notes

1. Some investigators have used concentrated instead of fuming sulfuric acid for the condensation, but the yield is usually low and the product is always colored bright yellow by some impurity which cannot be removed by crystallization.

2. The time allowed for condensation may be shortened to one-half, without affecting the yield, by maintaining the temperature at 125–130° for this length of time.

3. Other Methods of Preparation

β-Methyl anthraquinone has been obtained by the oxidation of β-methyl anthracene by several investigators;[1] and material of the same origin, obtained by the benzene-extraction of crude commercial anthraquinone,[2] has been fully described. As regards the synthesis from phthalic anhydride and toluene, both the preparation and properties of *p*-toluyl-*o*-benzoic acid[3] and the complete synthesis[4] have been the subject of several papers. This acid has also been prepared from *o*-carbomethoxy benzoyl chloride and toluene.[5] The phthalic anhydride synthesis of anthraquinone derivatives in general has received considerable attention. An account of this work, together with extensive references, is given by Barnett.[6]

The following unimportant preparative methods may be mentioned: the production of β-methyl anthraquinone by the reduction of 2-bromo-3-methyl anthraquinone;[7] the oxidation of β-methyl anthracene-γ-carboxylic acid;[8] and the reduction of 2-methyl anthraquinonyl-1-diazonium sulfate.[9]

[1] Ber. **8**, 675 (1875); J. prakt. Chem. [2] **79**, 560 (1909); [2] **82**, 232 (1910); [2] **83**, 210 (1911); Ann. chim. phys. [8] **20**, 445 (1910).

[2] J. Chem. Soc. **65**, 843 (1894); Ber. **10**, 1485 (1877); **15**, 1820 (1882); **16**, 696, 1632 (1883).

[3] Bull. soc. chim. [2] **35**, 505 (1881); [3] **17**, 969 (1897); Ann. chim. phys. [6] **14**, 447 (1888); Monatsh. **32**, 639 (1911); J. Am. Chem. Soc. **43**, 1965 (1921).

[4] J. prakt. Chem. [2] **33**, 319 (1886); [2] **41**, 4 (1890); Ann. **234**, 239 (1886); **299**, 300 (1898); **311**, 180 (1900); Ber. **28**, 1134 (1895); **41**, 3632 (1908); J. Russ. Phys. Chem. Soc. **46**, 1067 (1914).

[5] J. Am. Chem. Soc. **43**, 1922 (1921).

[6] Anthracene and Anthraquinone, pp. 130–141, Van Nostrand (1921).

[7] Ber. **45**, 796 (1912).

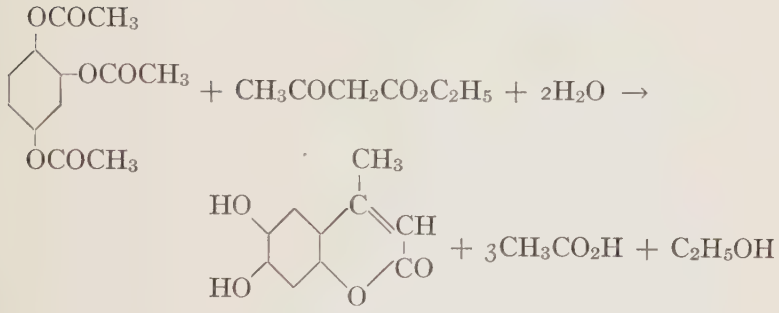
[8] Ber. **45**, 1214 (1912).

[9] Ber. **46**, 1646 (1913).

XVII

β-METHYL ESCULETIN

(6, 7-Dihydroxy-4-methyl-1, 2-benzopyrone)



Prepared by E. B. Vliet.
Checked by Roger Adams and E. E. Dreger.

1. Procedure

A smooth, uniform paste is made by thoroughly mixing 60 g. of ethyl acetoacetate (Note 1) and 114 g. of hydroxyhydroquinone triacetate (p. 35). This requires several minutes of stirring. To this mixture is added 450 cc. of 75 per cent sulfuric acid (Note 2). The paste slowly dissolves with the evolution of heat, giving a deep red solution; the latter is heated on a warm bath with occasional stirring until it reaches 80°, at which temperature it is maintained for one-half hour. It is then allowed to cool to room temperature and poured into 1850 cc. of cold water. The resulting mixture is cooled to room temperature, filtered with suction, and the precipitate washed with cold water to free it from excess acid. The β-methyl esculetin thus obtained is dried at 100° and is generally gray in color. The yield is about 80 g. (92 per cent of the theoretical amount).

A pure product may be obtained by dissolving with the aid of heat and stirring 100 g. of β-methyl esculetin in a solution of 200 g. of borax in 700 cc. of water. The solution obtained is filtered while hot and then cooled, whereupon the esculetin borate separates (Note 3). This is filtered off and dissolved in 1800 cc. of water, and the solution thus obtained added to 50 g. of concentrated sulfuric acid in 500 cc. of water. β-Methyl esculetin separates and, after the mixture has been cooled, is filtered, washed, and dried. From 100 g. of the crude material, 85 g. of pure product melting at 272–274° (uncor.) is obtained. This is generally nearly colorless but occasionally possesses a slight grayish tinge.

2. Notes

1. In order to obtain a fairly pure product without recrystallization, the intermediate ethyl acetoacetate and hydroxyhydroquinone triacetate must be pure.

2. It is important to use 75 per cent sulfuric acid in this reaction, because more concentrated acid gives a very dark product and a lower yield, while more dilute acid will not induce the reaction.

3. The exact nature of the precipitate has not been determined.

3. Other Methods of Preparation

β-Methyl esculetin was first prepared by Pechman,[1] by condensing hydroxyhydroquinone triacetate and ethyl acetoacetate by allowing them to stand for twenty-four hours with cold concentrated sulfuric acid. This method gave a dark product, difficult to purify, and a yield of 60–65 per cent. Pechman also used boiling alcoholic zinc chloride as the condensing agent in place of sulfuric acid but does not state the yield thus obtained.

Bargellini and Martegiani[2] used 73 per cent sulfuric acid and heated on the water bath. They obtained an improved yield of a product of better quality. Zinc chloride in acetic acid proved to be unsatisfactory.

[1] Ber. **34**, 423 (1901).

[2] Gazz. chim. ital. **41** (2), 613 (1911).

XVIII

METHYLENE AMINOACETONITRILE

(α-Hydroformamine Cyanide *)

$$NaCN + NH_4Cl + 2HCHO \rightarrow CH_2{=}NCH_2CN + NaCl + 2H_2O$$

Prepared by Roger Adams and W. D. Langley.
Checked by H. T. Clarke and E. R. Taylor.

1. Procedure

In a 5-l. round-bottom flask, fitted with a mechanical stirrer and surrounded by an ice-salt bath, are placed 1500 cc. of technical formaldehyde (sp. gr. 1.078/20°) (Note 1) and 540 g. of ammonium chloride. A thermometer is placed in the liquid, which is cooled to 0°. This temperature is maintained throughout the entire reaction (Note 2). Stirring is commenced (Note 3) and a solution of 490 g. of 98 per cent sodium cyanide in 850 cc. of water is dropped into the mixture of ammonium chloride and formaldehyde at such a rate (about 90 drops per minute) that at least six hours will be required for this addition.

When one-half the sodium cyanide solution has been added, all of the ammonium chloride will be in solution. At this point, the addition of 380 cc. of glacial acetic acid is started at such a rate (2 to 2.5 cc. per minute) that the addition of both the acid and the remainder of the sodium cyanide solution will be completed at the same time. The methylene aminoacetonitrile begins to separate in white crystals shortly after the addition of the glacial acetic acid has commenced. After all the sodium cyanide solution and acetic acid have been added, the mixture is stirred for an hour and a half longer; then the precipitate

* The actual molecular formula is $C_9H_{12}N_6$. Johnson and Rinehart, J. Am. Chem. Soc. **46**, 768, 1653 (1924).

is filtered off, transferred to a beaker, and stirred with 1.5 l. of water. The product is filtered with suction, washed with 500 cc. of water (Note 4), and dried on filter paper. The yield is 410 to 475 g. (64–74 per cent of the theoretical amount) of a product of which the melting point is 129° (Note 5).

2. Notes

1. The formalin contains 35 per cent formaldehyde by weight, as determined by specific gravity. It should contain no suspended paraformaldehyde.

2. During the reaction, the temperature should be kept as near 0° as possible and should never rise above 5°. If the temperature goes higher, a heavy oil is sometimes obtained instead of the crystalline product. It is not difficult to maintain the low temperature when the formaldehyde and ammonium chloride are cooled to 0° before any of the sodium cyanide is added.

3. In order to obtain good yields, the stirring must be vigorous throughout the entire reaction.

4. With careful washing, 500 cc. of cold water should be sufficient to remove all chlorides.

5. For most purposes, the product is pure enough as it is obtained from the reaction mixture, but it may be crystallized from water. This recrystallization is, however, attended with considerable loss.

3. Other Methods of Preparation

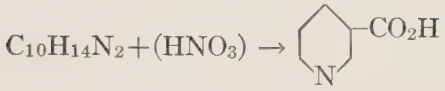
Methylene aminoacetonitrile has been prepared by the action of formaldehyde on aminoacetonitrile,[1] and by the action of formaldehyde on a mixture of ammonium chloride, potassium cyanide, and acetic acid.[2]

[1] J. prakt. Chem. (2) **65**, 192 (1902).

[2] Ber. **27**, 59 (1894); **36**, 1507 (1903); **43**, 868 (1910); J. Am. Chem. Soc. 768, 1653 (1924).

XIX

NICOTINIC ACID



Prepared by S. M. McElvain.
Checked by J. B. Conant and B. B. Corson.

1. Procedure

In a 5-l. round-bottom flask is placed 4 kg. of c.p. concentrated nitric acid (sp. gr. 1.42) (Note 1). To this is added, in 25-cc. portions, 210 g. of nicotine (Note 2). The addition should be made carefully in order that local heating may not occur and material be lost. After each addition of nicotine, the flask should be shaken in order to insure a homogeneous solution. The addition of the nicotine causes the temperature of the liquid to rise somewhat but not sufficiently to cause evolution of nitrogen dioxide. The flask is placed on a steam bath under a hood and heated until the liquid reaches a temperature of 70°. It is then removed and the reaction allowed to continue spontaneously (Note 3), heat enough being evolved to cause the liquid to boil. The boiling ceases after one hour but the flask is replaced upon the steam bath for ten to twelve hours, during which time there is a more or less continuous evolution of oxides of nitrogen.

The contents of the flask are then poured into an evaporating dish and evaporated almost to dryness on the steam bath (about ten hours). The purification which follows is best carried out with the product of two runs such as have been described above.

After the evaporation of most of the liquid, the nicotinic acid nitrate from two runs is transferred to a 1.5-l. beaker, 400 cc. of distilled water is added (Note 4) and the mixture is heated until complete solution results. On cooling, the nicotinic acid nitrate separates as yellow granular crystals and is

filtered off. To obtain it absolutely pure, it may be recrystallized in a way similar to that just described but with the use of bone-black. It contains one molecule of water of crystallization and has a melting point of 190–192° (cor.). The yield is 420–460 g. (85–91 per cent of the theoretical amount).

The 420–460 g. of crude nicotinic acid nitrate from two runs (not necessarily dry) is dissolved in 900 cc. of boiling water in a 3-l. beaker and 800 g. of crystalline disodium phosphate ($Na_2HPO_4 \cdot 12H_2O$) added with constant stirring. The resulting thick mixture is stirred and heated almost to boiling for five minutes and then allowed to cool. The mixture is finally chilled to 0° by an ice bath. It is well to stir occasionally during the crystallization to prevent the formation of too solid a cake of crystalline material. The nicotinic acid is filtered off upon a 15-cm. Büchner funnel and washed with three 100-cc. portions of cold water.

The yield is 260–300 g. of material containing a small amount of mineral salts but otherwise nearly pure. It can be purified further by recrystallization from 2.5 to 3.5 l. (Note 4) of hot water, 150–180 g. of material, which melts at 230–232° (cor.), being obtained. The yield of recrystallized material is 50–60 per cent of the theoretical amount, based upon the nicotine employed.

The recrystallization is the least satisfactory part of this procedure and involves the greatest apparent loss of material; the product before recrystallization is sufficiently pure for most purposes. By evaporation of the mother liquors, 40–45 g. of pure nicotinic acid may be obtained, making the total yield of pure material 190–225 g. (63–74 per cent of the theoretical amount); in addition, a small amount of somewhat less pure material is recovered.

2. Notes

1. Fuming nitric acid, the use of which is advised in the literature, is not as convenient to use and gives no better results than concentrated nitric acid.

2. A product of 100 per cent purity gives no better results

than does the crude 95 per cent material used in this experiment. The nicotine was purchased from the Hall Tobacco Company, of St. Louis, Mo.

3. If the nicotine and nitric acid mixture is merely placed on a steam bath and allowed to heat without control of the temperature, an occasional run will react violently, with loss of material.

4. The amounts of solvent given for the various recrystallizations are those which give best yields and it is advisable to follow them as closely as possible.

5. Nicotinic acid hydrochloride may be obtained directly from the nitrate by heating on a steam bath 460 g. of crude nitrate with 1000 cc. of concentrated hydrochloric acid (sp. gr. 1.19). After six to eight hours, the evolution of gas ceases and the liquid is evaporated under diminished pressure. The dry salt is again treated with 500 cc. of hydrochloric acid and heated for five hours and then evaporated as before.

After the salt has been again obtained, it is dissolved in 400 cc. of hot water and the solution diluted with four times its volume of 95 per cent alcohol. Upon cooling and stirring, the hydrochloride, melting at 273–274°, is obtained in a yield of 245–250 g. An additional quantity of 75–80 g. may be obtained from the mother liquors.

3. Other Methods of Preparation

Nicotinic acid has been prepared by the oxidation of nicotine with nitric acid.[1] It has also been prepared by the action of potassium permanganate upon β-picoline, nicotine, lutidine, β-phenyl pyridine, and β-dipyridyl [2] and by the action of chromic acid upon nicotine and β-phenyl pyridinecarboxylic acid.[3]

It may also be obtained by heating quinolinic acid [3] and certain other pyridine dicarboxylic acids.[2] The nitrile has been prepared by heating sodium β-pyridinesulfonate with potassium cyanide.[4]

[1] Ann. **165**, 330 (1873); Ber. **34**, 702 (1901); Chem. Zentr. **1898** (I), 677.
[2] Beilstein **4**, 143 (1899); **4***, 108 (1906).
[3] Rec. trav. chim. **1**, 121 (1882); Arch. Pharm. **240**, 353 (1902).
[4] Ber. **15**, 63 (1882).

XX

PENTAERYTHRITOL

(Tetra-hydroxymethyl methane)

$$8CH_2O + 2CH_3CHO + Ca(OH)_2 \rightarrow 2C(CH_2OH)_4 + (HCO_2)_2Ca$$

Prepared by Chemical Laboratory, Picatinny Arsenal.
Checked by H. T. Clarke and Ross Phillips.

1. Procedure

In a 6-gal. crock provided with an efficient stirrer are placed 10.5 l. of water, 5600 g. commercial (35–40 per cent) formaldehyde, and 630 g. of acetaldehyde (b.p. 20–22°). To this mixture is added, during the course of one-half hour, with constant mechanical stirring, 475 g. of high-grade quicklime to which enough water has been added to cause the disintegration of lumps by slaking. This lime must be in the form of a fine powder (Note 1). During the addition, the temperature of the mixture is raised by injection of live steam (Note 2) to 60–65°, and is held at this point for two hours after all has been added (Note 3).

The mixture is then cooled by surrounding the crock with cold water, and about 1700 g. of cold 50 per cent sulfuric acid is added, until a filtered sample just fails to yield a further precipitate of calcium sulfate upon the further addition of sulfuric acid. The calcium sulfate is filtered off and washed with cold water. A saturated aqueous solution of oxalic acid is cautiously added to the filtrate until a filtered sample gives no test for calcium salts in solution (Note 4).

The resulting solution, which should now be clear and lemon yellow in color (Note 5), is concentrated under reduced pressure on the steam bath (Note 6, Fig. 3) until the volume is reduced

to 3.5–4 l. It is then cooled and the crystalline precipitate filtered off by suction and washed with methyl alcohol or 95 per cent ethyl alcohol (Note 7) in small portions, until the washings are colorless. The product thus obtained weighs 900–960 g. and melts without decomposition at 250–252° (Note 8). The mother liquor and washings are further concentrated (Note 9) to a syrup, from which a second crop of 100–250 g. is obtained upon cooling. This is washed as before with alcohol but pos-

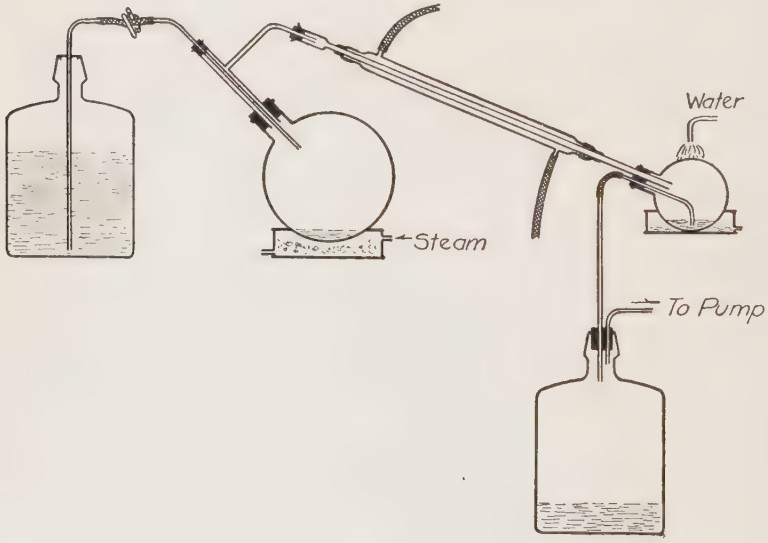


FIG. 3.

sesses a slightly yellow color and must be recrystallized from an equal weight of water. The total yield of product of m.p. 250–252° is 975–1055 g. (50–54 per cent of the theoretical amount).

2. Notes

1. The quicklime may be ground mechanically before addition, but this is less convenient than disintegrating it by the cautious addition of water.

2. If mechanically powdered quicklime is used, the use of steam is unnecessary, and the temperature is to be controlled

by the rate of addition. The use of heating and cooling coils in the crock is most convenient if available; such coils may safely be of iron tubing. Temperatures above 65° result in a lower yield of less pure product.

3. After the mixture has been maintained at 60–65° for a period of about one hour, the initial gray color undergoes a rapid change to yellow. This change is accompanied by a marked diminution in the odor of aldehydes.

4. The presence of only a slight excess of oxalic acid is permissible, although it is essential to remove all calcium salts since they would contaminate the final product; but small quantities of free oxalic acid do not interfere with the subsequent operations and are removed in the mother liquors.

5. The liquor may profitably be treated with decolorizing carbon at this point.

6. The apparatus shown in Fig. 3 has been found convenient for such evaporations under reduced pressure. The distillation is started with 3.5–4 l. in the 12-l. flask, and the level of liquid is maintained by controlling the rate of addition by means of a screw clamp. A 2-l. flask has been found satisfactory for the condensing intermediate receiver, provided the outside be completely wetted by the cold water.

7. Nearly 1 l. of ethyl alcohol is required. Pentaerythritol is insoluble in the cold alcohol, which dissolves the sticky polymerized aldehydes obtained on concentrating the solution.

8. The product is sufficiently pure for most purposes, but may be recrystallized from slightly more than an equal weight of boiling water.

9. The washings may be collected separately and the alcohol recovered by distillation from a steam bath under slightly reduced pressure.

3. Other Methods of Preparation

The only practicable process for the preparation of pentaerythritol consists in condensing acetaldehyde with formaldehyde in dilute aqueous solution by means of calcium (or barium)

hydroxide;[1] it has, however, also been formed by the action of sodium amalgam upon the pentaerythrose produced by condensing acetaldehyde with formaldehyde by means of sodium hydroxide.[2]

[1] Ann. **265**, 316 (1891); Ann. **276**, 58 (1893); C. A. **11**, 2543 (1917); D. R. P. 390,622; Chem. Zentr. **1924** (1) 2396.

[2] Am. Chem. J. **37**, 38 (1907).

XXI

β-PHENYLHYDROXYLAMINE

$$C_6H_5NO_2 + 2Zn + H_2O \rightarrow C_6H_5NHOH + 2ZnO$$

Prepared by Oliver Kamm.
Checked by C. S. Marvel.

1. Procedure

In a 4-gal. earthenware jar are placed 250 g. of technical ammonium chloride, 8 l. of water, and 500 g. of nitrobenzene. The mixture is stirred vigorously by means of a mechanical stirrer, and 620 g. of zinc dust of 85 per cent purity is added (Note 1) during the course of fifteen to twenty minutes (Note 2). As the reduction proceeds, the temperature rises to 60–65°. Stirring is continued for fifteen minutes after all the zinc dust has been added, at the end of which time the reaction is complete, as indicated by the fact that the temperature of the mixture ceases to rise.

While still hot, the solution is filtered with suction in order to remove the zinc oxide, which is washed with 1 l. of hot water. The filtrate is placed in an enamelled pan, saturated with salt, about 3 kg. being required, and cooled to 0° by being placed in an ice-salt mixture. The phenylhydroxylamine, which crystallizes out in long, light yellow needles (Note 3), is filtered by suction. The yield of crude product varies considerably, depending upon the amount of salt solution present, but averages 350–400 g. This corresponds to 275–300 g. (62–67 per cent of the theoretical amount) of actual phenylhydroxylamine, as determined by its separation from inorganic materials by solution in ether (Note 4).

Since phenylhydroxylamine deteriorates upon storage, it is generally used promptly, as illustrated in the preparation of cupferron, p. 19. The oxalate is somewhat more stable.

2. Notes

1. The zinc dust must be analyzed (Gattermann, "Practical Methods of Organic Chemistry," 3rd ed., p. 390), and a proportional quantity used if the zinc content is not 85 per cent. Technical nitrobenzene is satisfactory if it distils over a range of not more than 5 degrees and is not acid in reaction.

2. When the reaction is run more slowly, the temperature does not reach 60–65° and the yield is poorer. At 50–55°, the yield is about 55 per cent.

3. It is important that the phenylhydroxylamine solution be kept at 0° for at least one-half hour or considerable material will be lost in the solution. The use of an enamelled pail saves a great deal of time at this step.

4. Phenylhydroxylamine is soluble in saturated salt solution at 0° to the extent of about 9 grams per liter, but this amount is not included in the yields given. Occasional yields of 300–310 g. of dry phenylhydroxylamine have been obtained.

3. Other Methods of Preparation

Although phenylhydroxylamine may be prepared by catalytic reduction,[1] by the oxidation of aniline,[2] and by electrolytic reduction of nitrobenzene,[3] the most feasible method is still based upon the original zinc reduction method of Bamberger [4] and of Wohl.[5] Various solvents and catalysts have been used in this reduction, and copper-coated and amalgamated zinc, as well as aluminium amalgam,[6] have been substituted for zinc dust. The method herein recommended is essentially one previously described [7] but it has been found [8] that cooling is not an essential, as claimed in the patents. The preparation of the oxalate is also a more recent contribution.[9]

[1] Ber. **55**B, 875 (1922). [2] Ber. **32**, 1676 (1899).
[3] Chem. Zentr. **1898** (II), 634; Z. physik. Chem. **32**, 272 (1900); J. Phys. Chem. **19**, 696 (1915).
[4] Ber. **27**, 1348, 1548 (1894). [5] Ber. **27**, 1432 (1894).
[6] Beilstein **2***, 241 (1903); J. Chem. Soc. **119**, 767 (1921); J. Ind. Eng. Chem. **12**, 799 (1920).
[7] D. R. P. 89,978; Frdl. **4**, 47 (1896). [8] J. Am. Chem. Soc. **41**, 277 (1919).
[9] U. S. Patent 1,390,260; C. A. **16**, 105 (1922).

XXII

n-PROPYLBENZENE

$$C_6H_5CH_2Cl + Mg \rightarrow C_6H_5CH_2MgCl$$

$$C_6H_5CH_2MgCl + (C_2H_5)_2SO_4 \rightarrow C_6H_5CH_2CH_2CH_3 + MgCl(SO_4C_2H_5)$$

Prepared by Henry Gilman and C. H. Meyers.
Checked by C. S. Marvel and H. O. Calvery.

1. Procedure

In a 5-l. flask standing in an empty water bath are placed 50 g. of clean magnesium turnings and 600 cc. of dry ether which has been distilled over phosphorus pentoxide and stored over sodium; the flask is then fitted with a stirrer having a mercury seal, a thermometer, an efficient reflux condenser, and a dropping funnel. About 50 cc. of a solution of 253 g. of benzyl chloride, boiling at 172–175°, in 800 cc. of dry ether is then added through the dropping funnel and the mixture heated just to boiling by placing in the bath enough water at 40° to cover about half the surface of that part of the flask which is in contact with the ethereal mixture.

As soon as the ether begins to boil, the warm water is siphoned out; if the boiling should continue vigorously, owing to the reaction having set in, the rate may be regulated by placing cold water in the bath. The remainder of the benzyl chloride solution is then added at such a rate that the mixture boils gently; this will require about four hours. When all has been added, stirring is commenced and the mixture gently boiled for fifteen minutes by the gradual replacement of the cold water by warm.

The temperature of the mixture is then lowered by means of running water, and 385 g. of C. P. ethyl sulfate (Note 1) is dropped in, with continuous stirring, during one and a half hours, allowing the temperature to rise gradually. When all has been added, stirring is continued with gentle boiling for an hour. The cooled mixture is then poured cautiously, with stirring, upon a mixture of 1 kg. of crushed ice, 1 kg. of water, and 200 cc. of concentrated hydrochloric acid.

After a few minutes, the bulk of the water layer is removed by a siphon and the clear ethereal solution decanted, so far as possible, into a 2-l. flask. The remaining mixture is filtered through a glass-wool plug into a separatory funnel, and after removal of the aqueous portion, the remaining ethereal solution is added to that in the flask. An efficient fractionating column is attached, and the ether distilled on the water bath; the residue is then fractionated and collected as pure *n*-propylbenzene boiling at 154–158°. The yield is 133–156 g. (55–65 per cent of the theoretical amount).

2. Notes

1. The technical grade of diethyl sulfate gives poorer yields on account of the presence of free acid. The C. P. grade was used in order to obtain the results given in the procedure.

3. Other Methods of Preparation

n-Propylbenzene has been prepared by the action of sodium on a mixture of propyl bromide and bromobenzene,[1] of zinc dust upon a benzene solution of allyl bromide,[2] and of zinc ethyl upon benzyl chloride;[3] and aluminium chloride has been employed to condense benzene with propyl bromide,[4] allyl

[1] Ann. **149**, 324 (1869).

[2] Jahresb. **1895**, 1516; Bull. soc. chim. (3) **16**, 126 (1896).

[3] Ber. **10**, 294 (1877); Gazz. chim. ital. **7**, 21 (1877).

[4] Ber. **24**, 768 (1891); J. Russ. Phys. Chem. Soc. **27**, 457 (1895); Bull. soc. chim. (3) **16**, 864 (1896).

chloride [5] and trimethylene bromide,[6] but the tendency of this reagent to induce isomerization is a distinct danger.

n-Propylbenzene has also been obtained by the action of hot sulfuric acid upon a mixture of propyl alcohol and benzene.[7] Reduction methods have been applied to various monosubstituted benzene derivatives possessing a three-carbon-chain, namely, phenyl ethyl ketone and benzyl methyl ketone,[8] γ-phenyl *n*-propyl chloride or bromide,[9] propenylbenzene,[10] phenyl ethyl ketoxime [11] and cinnamyl alcohol or phenyl allyl alcohol.[12]

[5] Ann. **218**, 379 (1883); Bull. soc. chim. (2) **41**, 197 (1884); (2) **43**, 588 (1885).
[6] Compt. rend. **132**, 155 (1901).
[7] Compt. rend. **117**, 236 (1893).
[8] J. prakt. Chem. (2) **81**, 387 (1910); Ber. **46**, 1839 (1913).
[9] Ber. **43**, 178 (1910); **44**, 2872 (1911); **45**, 2176, 2179 (1912).
[10] Ber. **36**, 622, 773 (1903).
[11] Bull. soc. chim. (4) **9**, 465 (1911).
[12] Ber. **39**, 2590 (1906).

XXIII

PYRUVIC ACID

$$\begin{matrix}\mathrm{CHOHCO_2H}\\ |\\ \mathrm{CHOHCO_2H}\end{matrix} + (\mathrm{KHSO_4}) \rightarrow \mathrm{CH_3COCO_2H} + \mathrm{H_2O} + \mathrm{CO_2}$$

Prepared by J. W. Howard and W. A. Fraser.
Checked by C. S. Marvel and R. L. Shriner.

1. Procedure

An intimate mixture of 600 g. of finely powdered freshly *fused* potassium acid sulfate and 400 g. of powdered tartaric acid, prepared by grinding them together in a mortar, is placed in a 3-l. round-bottom Pyrex flask connected with a condenser which is filled with water but does not have any water flowing through it. The mixture is heated by means of an oil bath maintained at a temperature between 210 and 220° until liquid no longer distils over. Some foaming takes place (Note 1), but if fused potassium acid sulfate is used and the temperature of the bath does not rise above 220°, it is not difficult to control. The distillate is then fractionated under reduced pressure. Pyruvic acid passes over at 75 80°/25 mm. and the yield is 117–128 g. (50–55 per cent of the theoretical amount).

2. Notes

1. If the mixture foams badly, it may be kept from frothing over by heating the upper part of the flask with a free flame.

2. The cake left in the reaction flask may be removed readily by inverting over a steam jet.

3. Other Methods of Preparation

Pyruvic acid has been prepared from α,α-dichloropropionic acid and from the corresponding dibromo acid, by heating with

water under pressure, by heating with barium hydroxide solution, and by the treatment of the aqueous solutions with silver oxide or silver carbonate.[1] The action of sodium hydroxide on α,α-dibromopropionic acid has also been studied.[2] Better results have been reported from the hydrolysis of acetyl cyanide and of oxalacetic ester.[3]

It has been obtained by the oxidation of lactic acid,[4] mesaconic acid and citraconic acid,[5] acetone and acetol,[6] but in general these oxidation procedures are not suitable as preparative methods.

Pyruvic acid may be obtained by the distillation of tartaric acid or glyceric acid.[7] Better results are obtained, however, by the distillation of tartaric acid in the presence of a dehydrating agent such as potassium bisulfate.[8] This method has been adopted after a study of a variety of dehydrating agents and various experimental procedures.

[1] Ber. **5**, 477 (1872); **10**, 264, 2037 (1877); **18**, 228, 235 (1885).

[2] Ann. **342**, 132 (1905).

[3] Ber. **11**, 620, 1563 (1878); Ann. **246**, 327 (1888).

[4] J. Chem. Soc. **77**, 71 (1900); Ber. **17**, 840 (1884); Chem. Met. Eng. **28**, 357 (1923).

[5] Ann. **305**, 48, 49 (1899).

[6] Compt. rend. **140**, 1592 (1905); Bull. soc. chim. (4) **3**, 259 (1908); Ber. **20**, 641 (1887); J. Am. Chem. Soc. **39**, 2661 (1917).

[7] Ann. physik. (2) **36**, 1 (1835); Ann. **131**, 338 (1864); **188**, 314 (1877).

[8] Ber. **14**, 321 (1881); Bull. soc. chim. (3) **13**, 335 (1895); Rec. trav. chim. **19**, 278 (1900); Ann. **242**, 269 (1887); Ber. **43**, 2188 (1910).

XXIV

SODIUM *p*-HYDROXYPHENYLARSONATE

$$C_6H_5OH + H_3AsO_4 \rightarrow HOC_6H_4AsO_3H_2 + H_2O$$

Prepared by W. G. Christiansen and A. J. Norton.
Checked by Oliver Kamm.

1. Procedure

Seven hundred and twenty grams of syrupy arsenic acid (75–80 per cent) is boiled in a beaker until the temperature of the acid is 150°; about 120 g. of water is driven off, leaving a syrup containing approximately 95 per cent of orthoarsenic acid, which is then added to 300 g. of phenol in a 1-l. round-bottom, short-neck Pyrex flask. By means of a 3-hole stopper, an efficient jacketed stirrer (Org. Syn. **1**, 4) and a thermometer are introduced into the flask, and a connection is established with a downward condenser. The flask is set in an oil bath which is heated at once to 155–160°, and the stirrer is run at a rate high enough to insure thorough mixing.

When the inside temperature reaches 140°, boiling commences and water plus a very little phenol begins to distil. The distillation is allowed to continue until 60 cc. (one molecular equivalent) of water has been collected; this usually requires one hour, and the inside temperature rises to 146°. The downward condenser is then replaced by a reflux condenser (Note 1) and the reaction is allowed to continue until a total of four hours has elapsed from the time the contents of the flask first reached 140°. After the return condenser has been attached, the inside temperature declines slowly to 141° or 142° and the reaction mixture becomes thicker and somewhat tarry. After the contents of the flask have been partially cooled, they are

poured into 4 l. of water and mechanically stirred; the agitation is continued for a short time in order to break up the tarry material and enable the water to dissolve the hydroxyphenylarsonic acids completely.

Finely ground barium hydroxide is added gradually to the well-stirred water solution until the material is slightly alkaline to litmus, in order to remove the excess of arsenic acid; when this point is reached, the solution becomes pink. If the procedure is carried out properly, 700–800 g. of $Ba(OH)_2 \cdot 8H_2O$ should suffice (Note 2). The time required by this method is greater than when a hot solution of barium hydroxide is used, but the method is more convenient and does not cause such a great increase in volume. After removal of the barium arsenate by filtration, the mother liquor and washings are treated with sulfuric acid until the solution contains neither barium nor sulfate ions. When the barium sulfate has been separated and thoroughly washed (Note 3), the filtrate is concentrated on a steam bath to about 3 l., neutralized to litmus with sodium hydroxide, filtered, evaporated until the solution becomes well coated with crystals, and then treated with 2.5 volumes of alcohol. After the mixture has cooled in an ice-box, the sodium *p*-hydroxyphenylarsonate is separated, washed with alcohol, and dried in an oven at 80°. A second crop may be secured from the filtrate by concentrating it further and precipitating with alcohol. The total yield of anhydrous sodium *p*-hydroxyphenylarsonate is 252 g. (33 per cent of the theoretical amount). By proper manipulation, it is possible to obtain as much as 240 g. in the first crop and to have it free from sulfate, arsenate, and sodium *o*-hydroxyphenylarsonate which is one of the by-products formed in this reaction (Note 4).

2. Notes

1. When the downward condenser is not replaced by a reflux condenser, the total volume of water that distils is 90–120 cc. and the mass becomes very tarry, owing to the oxidation of phenol or of some intermediate substance formed in the reaction.

p-Hydroxyphenylarsonic acid is not destructively oxidized by hot arsenic acid.

2. In removing the excess arsenic acid with barium hydroxide, the solution should not be permitted to become strongly alkaline, as the barium salt of the hydroxyphenylarsonic acid may commence to separate, thereby decreasing the yield.

3. The filtration of large quantities of barium sulfate is usually tedious; but if filtering carbon is added to the suspension to be filtered and if a mat of this carbon is prepared on the filter by filtering an aqueous suspension of carbon, the barium sulfate may be removed rapidly and completely, even when it is precipitated from cold solutions.

4. When phenol is arsonated with arsenic acid, small amounts of *o*-hydroxyphenylarsonic acid, *p*,*p*′-di-hydroxyphenylarsinic acid and *o*,*p*′-di-hydroxyphenylarsinic acid are formed as by-products. As the sodium salts of the secondary acids are soluble in alcohol, they will not appear in the material precipitated by the addition of alcohol. The sodium salt of *o*-hydroxyphenylarsonic acid, although insoluble in alcohol, will not be precipitated if the solution is not concentrated too far before addition of the alcohol. To test the material for the presence of the ortho compound, ferric chloride is added to an aqueous solution of a small amount of the solid; the ortho hydroxy acid gives a deep purple color, whereas the para acid gives no coloration. The sodium salt which is precipitated with alcohol contains water of crystallization, which is driven off by drying at 80°. The product can be purified by dissolving in hot water and adding hot alcohol until a slight permanent turbidity is produced. Upon cooling, the material separates in a crystalline condition. Occasionally, the second crops of sodium *p*-hydroxyphenylarsonate contain small amounts of arsenious oxide which is formed from the arsenic acid during the oxidation mentioned above.

3. Other Methods of Preparation

p-Hydroxyphenylarsonic acid may be prepared by diazotization of arsanilic acid and replacement of the diazo group by

hydroxyl.[1] The method of directly introducing the arsenic acid group into phenol is more satisfactory. This preparation was first described in the patent literature,[2] but the method proved unworkable and was reinvestigated and improved by Conant [3] and later by Jacobs and Heidelberger.[4] In the present method,[5] additional improvements have been effected.

[1] Ber. **41**, 1854 (1908).
[2] D. R. P. 205,616; Frdl. **9**, 1040 (1908).
[3] J. Am. Chem. Soc. **41**, 431 (1919).
[4] J. Am. Chem. Soc. **41**, 1440 (1919).
[5] J. Am. Chem. Soc. **45**, 2188 (1923).

XXV

o-TOLUNITRILE AND *p*-TOLUNITRILE

$$CH_3C_6H_4NH_2+HNO_2+HCl \rightarrow CH_3C_6H_4N_2Cl+2H_2O$$

$$CH_3C_6H_4N_2Cl+NaOH+NaCu(CN)_2 \rightarrow CH_3C_6H_4CN+N_2+NaCl+CuCN$$

Prepared by H. T. Clarke and R. R. Read.
Checked by C. S. Marvel and M. M. Brubaker.

1. Procedure

A. *Preparation of the cuprous cyanide solution:* Cuprous chloride prepared from 1250 g. of copper sulfate, according to the directions given in Org. Syn. **3**, 33, is suspended in 2 l. of cold water in a 15-l. crock fitted with a mechanical stirrer. A solution of 650 g. of sodium cyanide (96–98 per cent) in 1 l. of water is added and the mixture stirred, whereupon the cuprous chloride enters into solution with considerable evolution of heat (Note 1). The mixture is then cooled by surrounding the crock with cold water (Note 2).

B. *Preparation of o-tolunitrile:* While the cuprous cyanide solution is cooling, 428 g. of *o*-toluidine is mixed in a 20-l. crock with 1 l. of commercial 28 per cent hydrochloric acid (sp. gr. 1.14) and enough cracked ice, about 4 kg., to bring the temperature of the mixture to 0°. A solution of 280 g. of sodium nitrite in 800 cc. of water is added, with stirring, to the resulting suspension of *o*-toluidine hydrochloride, the temperature being kept at 0–5° by the addition of cracked ice. The addition of the nitrite occupies about fifteen minutes; at the end of the operation, the mixture must show a distinct and permanent reaction for free nitrous acid on testing with starch iodide paper (Note 3). The final volume of the solution is 5–6 l. The mixture is now

cautiously neutralized by adding dry sodium carbonate with constant stirring, using litmus paper to determine the end point; about 200 g. of the anhydrous carbonate is required (Note 4).

The cold cuprous cyanide solution is now chilled to 0–5° by the addition of ice, and 1 l. of benzene is poured on the surface. To this mixture is slowly added the cold neutralized diazonium solution. During the addition, which occupies about thirty minutes, such vigorous stirring is maintained that the benzene on the surface is constantly drawn to the stirrer, and the temperature is maintained at 0–5° by occasionally adding ice. As soon as the diazonium solution comes into contact with the cuprous cyanide, a dark yellow, oily precipitate is formed which at once begins to give off nitrogen; the resulting nitrile is taken up by the benzene as soon as it is formed (Note 5). When all has been added, the temperature is held at 0–5° for thirty minutes longer, and then is allowed to rise to that of the room (20–25°), which usually requires about three hours.

After stirring has been continued for two hours longer, the crock is surrounded by hot water or steam and warmed to 50° without stirring. The mixture is then allowed to stand until cool, when the aqueous layer is drawn off by means of a siphon. The upper oily layer is transferred to a 12-l. flask and distilled in a current of steam until no more oil passes over; about 10 l. of distillate is collected (Note 6). The water is drawn off and the benzene removed by distillation, by means of a 2-l. round-bottom flask and a fractionating column about 90 cm. long. When benzene no longer distils over, the distillation is continued in the same apparatus under reduced pressure, and the fraction that boils at 94–96°/20 mm. is collected. A small amount of dark-colored residue remains in the flask. The yield of almost colorless *o*-tolunitrile is 300–330 g. (64–70 per cent of the theoretical amount).

p-Tolunitrile can be prepared in exactly the same manner from *p*-toluidine; the product, which distils at 104–106°/20 mm., solidifies in the receiver to a mass of nearly colorless needles which melt at 25–27°. The yield is the same as with the ortho compound (Note 7).

2. Notes

1. If desired, the cuprous chloride may be suspended in 3 l. of water and the sodium cyanide added in the solid form.

2. If several runs are to be made it may be more convenient to prepare a large quantity of cuprous cyanide solution, since this appears to be stable for several days.

3. If the sodium nitrite is not of the highest technical purity it may be necessary to employ more than the indicated quantity. It is essential that the test for nitrous acid be permanent; if any unchanged amine remains, a precipitate of the diazoamino compound is formed on neutralization. A moderate excess of nitrite does not appear to interfere with the reaction, especially since the greater portion of the free nitrous acid is removed by the carbon dioxide liberated on neutralization.

4. Sodium carbonate is preferable to sodium hydroxide because very little heat is evolved on neutralization. A slight excess of carbonate does not appear to be harmful.

5. It is essential that the stirring be very vigorous. If the intermediate addition compound is allowed to collect on the surface of the liquid, it decomposes spontaneously with evolution of much heat; this decomposition may take place with almost explosive violence. The presence of the benzene tends to diminish the viscosity of the intermediate product and permit it to be readily distributed throughout the mixture. Decomposition is quite rapid at 0° and is practically complete when room temperature is reached; it appears, however, to be advisable to warm the mixture to 50°, since if this be omitted the yield is slightly decreased.

6. The apparatus described in Org. Syn. **2**, 80, is suitable for the steam distillation.

7. The product, as obtained in the above procedure, is of high purity; cresols do not appear to be formed under the conditions specified. The process has the advantage over that described in the literature [1] of giving rise to no poisonous fumes during the formation of the cuprous cyanide and during the interaction of this with the diazonium salt. The yield is practically the same as in the older method.

3. Other Methods of Preparation

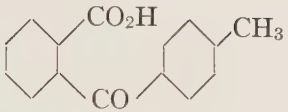
The original method of Sandmeyer [1] prescribed the preparation of the cuprous cyanide solution by dissolving copper sulfate in potassium cyanide solution and adding the strongly acid diazonium solution to it. Both of these operations involve the evolution of poisonous gases—cyanogen in the first case and hydrogen cyanide in the second. Slight modifications have been subsequently suggested: the use of a 50 per cent excess of cuprous cyanide [2] and the heating of the cuprous cyanide solution before the reaction.[3]

o-Tolunitrile has also been prepared from *o*-toluidine by conversion into *o*-tolyl isothiocyanate and the boiling of this under a reflux condenser; [4] *p*-tolunitrile has been prepared by distilling *p*-toluic acid with potassium thiocyanate; [5] and a mixture of the two has been produced by the interaction of toluene, mercury fulminate, and aluminium chloride.[6]

[1] Ber. **17**, 2653 (1884); **18**, 1492, 1496 (1885).
[2] Ber. **19**, 756 (1886).
[3] Ber. **23**, 1026 (1890).
[4] Ber. **6**, 419 (1873).
[5] Ber. **8**, 441 (1875).
[6] Ber. **36**, 14 (1903).

XXVI

p-TOLUYL-*o*-BENZOIC ACID

$$C_6H_4(CO)_2O + C_6H_5CH_3\ (Al_2Cl_6) \rightarrow$$ 

Prepared by L. F. Fieser.
Checked by Roger Adams and R. L. Shriner.

1. Procedure

A 2-l. round-bottom flask is clamped to a ring-stand and equipped with a rubber stopper protected with tin foil and carrying a glass stirrer with mercury seal and a reflux condenser. (Cf. Org. Syn. 1, 4, Fig. 1, *a*.) As an outlet for the hydrogen chloride, the top of the condenser is provided with a bent tube which almost touches the surface of the water in a half-filled 1-l. flask.

One hundred grams of phthalic anhydride and 400 g. of toluene are placed in the flask, which is cooled in an ice bath while 200 g. of anhydrous aluminium chloride (Note 1) is being ground to a fine powder. The chloride is now added all at once, and connections to the condenser made as rapidly as possible. Stirring is commenced at once and the ice bath is removed. The mixture warms up considerably and becomes olive-green in color. When the evolution of hydrogen chloride begins to slacken (ten minutes) a water bath is put into place and heated to 90° in the course of forty-five minutes. The temperature of the bath is kept at 90° and vigorous stirring continued for two and one-half hours. At this point, the evolution of hydrogen chloride will have practically ceased and the reaction will have been completed. The hot water in the bath is replaced first by cold water and then by ice, while stirring is continued.

As soon as the flask is well cooled, it is disconnected and carried to the hood, and ice is slowly added, with shaking, until the dark mass is completely decomposed and the flask is about half filled with the mixture. After 150 cc. of crude concentrated hydrochloric acid has been added, the mass coagulates and the solution clears; the flask is then heated on the steam bath while preparations are being made for steam distillation.

This operation, which removes the excess of toluene, may be carried out in the same flask and loss by transfer thus avoided (Note 2). The aqueous solution of aluminium chloride and hydrochloric acid, after thorough cooling, is decanted through a suction filter, the residue washed with a little cold water, and that collected on the filter returned to the flask. This residue consists almost solely of toluylbenzoic acid, partly crystalline, partly in oily lumps.

A previously prepared and heated solution of 50 g. of sodium carbonate in 1 l. of water is added, and steam is passed in to provide heat and agitation. With a rapid stream, the acid will go into solution in about ten minutes, leaving a small amount of brown, tarry material and a little alumina undissolved (Note 3). The solution is filtered while hot and transferred to a 2-l. beaker, and the acid precipitated by the addition of 65 cc. of concentrated hydrochloric acid. The acid separates as an oil, which soon crystallizes. The solution is cooled in ice and the acid filtered and washed.

The air-dried product is pure white and weighs 170 g. (Note 4). After drying at 100°, the anhydrous acid melts at 138–139° and weighs 157 g. (96 per cent of the theoretical amount). Air-dried material is suitable for the condensation to β-methyl anthraquinone, p. 43. It may be recrystallized from toluene.

2. Notes

1. Although statements are found in the literature that quantitative yields may be obtained with smaller quantities of aluminium chloride, the ratio $1C_6H_4(CO)_2O : 1Al_2Cl_6$ is essential.

2. The steam distillation requires about fifteen minutes, and about 340–380 cc. of toluene is recovered.

3. If, in extracting the acid with sodium carbonate, more than 2–3 g. of material remains undissolved, the residue is treated with dilute hydrochloric acid to remove alumina, washed, and again extracted with a little carbonate solution. This extract is neutralized separately since some tar may separate with the toluyl benzoic acid. In this event, it is filtered and extracted with *cold* carbonate solution, in which the tar is completely insoluble.

4. According to Limpricht, the acid may crystallize either in hydrated or in the anhydrous condition, but the transition temperature is not stated. The loss of water upon drying at 100° shows the compound obtained in this experiment to be the monohydrate.

3. Other Methods of Preparation

The only practical method for the preparation of *p*-toluyl-*o*-benzoic acid is that proposed by Friedel and Crafts.[1] Limpricht [2] has proposed a decrease in the quantity of aluminium chloride, but Heller and Schulke [3] and McMullen [4] have verified the importance of an excess of the condensing agent.

[1] Ann. chim. phys. (6) **14**, 447 (1888).
[2] Ann. **299**, 300 (1898).
[3] Ber. **41**, 3632 (1908).
[4] J. Am. Chem. Soc. **43**, 1965 (1921).

XXVII

TRICARBALLYLIC ACID

$$CH(CO_2C_2H_5)_2CH(CO_2C_2H_5)CH_2CO_2C_2H_5+4H_2O+(HCl) \rightarrow CH_2(CO_2H)CH(CO_2H)CH_2CO_2H+CO_2+4C_2H_5OH$$

Prepared by H. T. Clarke and T. F. Murray.
Checked by C. S. Marvel and M. M. Brubaker.

1. Procedure

In a 3-l. flask, fitted with a stirrer and a fractionating column with condenser for downward distillation, are placed 912 g. of ethyl propane-1,1,2,3-tetracarboxylate (p. 29) and 950 cc. of a solution of equal volumes of pure concentrated hydrochloric acid and distilled water. A receiver with a side-tube is attached to the condenser; this side-tube leads to a water trap. The mixture is boiled, with continual stirring, at such a rate that the alcohol is removed as fast as it is formed, but without undue removal of water from the flask (Note 1). The progress of the reaction can be followed by noting the rate at which carbon dioxide passes through the trap. When the temperature at the head of the column approaches 100°, the flame is turned down so that very little liquid distils over. Heating is continued until evolution of carbon dioxide ceases (Note 2).

The flask is now disconnected from the stirrer and column, and the contents distilled off as completely as possible on the steam bath under reduced pressure. The remaining solid is freed from residual moisture and hydrochloric acid by allowing a slow current of dry air to pass over it, while still heating on the steam bath and maintaining a partial vacuum (Note 3). It is then redissolved in distilled water, and the solution filtered with

the use of decolorizing carbon, and again evaporated under reduced pressure.

The residue, when completely dry, is ground up, mixed to a paste with dry ether, filtered by suction, washed with dry ether and dried. The product so obtained (Note 4) is practically pure and melts at 160–161°. The yield is 474–479 g. (95–96 per cent of the theoretical amount).

2. Notes

1. The temperature at the head of the column will give some idea of the relative amount of water passing over with the alcohol, but allowance must be made for the lowering of the distilling temperature by the carbon dioxide evolved.

2. Twelve hours' heating is necessary to complete the reaction.

3. The dry air is best introduced through a tube leading to the bottom of the flask; it is well not to disconnect the condenser, but to note the point at which no more drops condense. The current of dry air should be quite slow—not more than two bubbles per second in the sulfuric acid wash bottle.

4. Tricarballylic acid is readily soluble in water (requiring about twice its weight at room temperature), but may, if desired, be recrystallized from it. Dry ether may also be employed, about 50 parts by weight being necessary.

3. Other Methods of Preparation

Tricarballylic acid was originally prepared by hydrolysis of the nitrile obtained from glycerol tribromohydrin and potassium cyanide; [1] it has also been obtained by the reduction of aconitic acid by sodium amalgam [2] or electrolytically.[3] The hydrolysis of ethyl propanetetracarboxylate may be carried out either in acid solution (with hydrochloric acid)[4] or in alkaline solution,[5]

[1] Proc. Roy. Soc. **12**, 237 (1862); Ann. **128**, 352 (1863); Ann. **136**, 272 (1865).
[2] Ann. **132**, 62 (1864); Ber. **22**, 2920 (1889); Ann. **314**, 15 (1901).
[3] Compt. rend. **136**, 1331 (1903).
[4] Ber. **24**, 2889 (1891); Ann. **341**, 102 (1905).
[5] Ber. **23**, 3760 (1890); J. prakt. Chem. (2) **45**, 56 (1892).

the former being the more convenient. Tricarballylic acid is also formed by the acid hydrolysis of the less accessible methyl propanepentacarboxylate [6] and methyl propanehexacarboxylate,[7] as well as by the alkaline hydrolysis of acetyl tricarballylic ester.[8] Finally, it has been obtained by the oxidation of diallylacetic ester with nitric acid [9] and of gallic acid with potassium chlorate and hydrochloric acid.[10]

[6] Ber. **29,** 1742 (1896); Ann. **347,** 7 (1906).
[7] Ber. **29,** 1279 (1896).
[8] Ann. **190,** 324 (1878); Ber. **23,** 3756 (1890).
[9] Ann. **201,** 53 (1880).
[10] Ann. **177,** 292 (1875).

XXVIII

TRIPHENYLMETHANE

$$3C_6H_6+CCl_4+AlCl_3 \rightarrow (C_6H_5)_3CCl\cdot AlCl_3+3HCl$$

$$(C_6H_5)_3CCl\cdot AlCl_3+(C_2H_5)_2O \rightarrow (C_6H_5)_3CH+CH_3CHO+C_2H_5Cl+AlCl_3$$

Prepared by J. F. Norris.
Checked by H. T. Clarke and T. F. Murray.

1. Procedure

To a mixture of 292 g. of dry benzene and 116 g. of dry carbon tetrachloride, (Note 1) in a 1-l. flask provided with a reflux condenser having a calcium chloride tube at its upper end, is added 100 g. of anhydrous aluminium chloride in lumps (Note 2). The flask is at once immersed in ice-water to within 5 cm. of the top, and allowed to stand for twenty-four hours, the temperature of the water being allowed to rise to that of the room (Note 3). One hundred and ten grams of anhydrous ether is added in small portions, through the condenser, the flask being shaken occasionally during twenty minutes. The mixture is allowed to stand for twenty-four hours, and is then poured into a 5-l. flask containing 650 g. of ice and 25 cc. of concentrated hydrochloric acid. One liter of benzene is then added, and the mixture heated on a steam bath under a return condenser. After gently boiling for five to ten minutes, the mixture is allowed to cool to 40–50°, when the benzene layer is separated, washed with 700 cc. of warm water containing 25 cc. of concentrated hydrochloric acid, and distilled. After the benzene has been removed under atmospheric pressure, the residue is transferred to a 300-cc. flask and distilled under reduced pressure, and a

fraction boiling over the range 190–215°/10 mm. collected (Note 4). This weighs 135–160 g.; it solidifies on cooling. It is recrystallized from 550–650 cc. of ethyl alcohol (Note 5), and a colorless product, crystallizing in needles which melt sharply at 92°, is obtained. This is filtered off and washed twice with 30-cc. portions of fresh alcohol. The alcoholic mother liquor is concentrated and the residue distilled under reduced pressure, material which distils over at 190–200°/10 mm. being collected. This is recrystallized from ethyl alcohol, and 6–7 g. more of pure material is thus obtained. The total yield is 125–154 g. (68–84 per cent of the theoretical amount).

2. Notes

1. A convenient method for removing moisture from the carbon tetrachloride and the benzene consists in distilling off about one-tenth of the liquid; this first fraction contains all the moisture which may have been dissolved in the commercial products. It is, as a rule, unnecessary to distil the remaining liquid before use.

2. The aluminium chloride may be a good grade of technical anhydrous material. If a powdered product be employed, the reaction is apt to proceed too rapidly. The lump material appears to be somewhat more efficient.

3. With shorter periods of standing and lower temperatures, the yield falls off materially. Thus in one experiment in which the mixture was allowed to stand for twenty-four hours at 5–8°, a large proportion of a lower-boiling product (apparently diphenylmethane) was formed, and only 109 g. of crude triphenylmethane was obtained.

4. A dark, tarry residue amounting to 25–40 g. remains in the flask.

5. Methyl alcohol may also be employed, but it is necessary to use 1600–1700 cc. of it. Triphenylmethane dissolves in one-third of its weight of warm benzene; it separates from this solution with benzene of crystallization, which is lost on exposure to air or recrystallization from alcohol.

3. Other Methods of Preparation

The process here described consists essentially in the formation of triphenylchloromethane by the interaction of carbon tetrachloride and benzene in the presence of aluminium chloride, and the reduction of this product by ether under the influence of the aluminium chloride present.

Triphenylchloromethane is most satisfactorily prepared by the above method,[1] though ferric chloride may also be employed as a catalyst.[2] Its reduction by means of ether was first observed by Gomberg,[3] the catalyst in this case being zinc chloride; it had previously been shown [4] that triphenylchloromethane (or triphenylcarbinol) is reduced to triphenylmethane by means of alcohol in the presence of sulfuric acid.

Triphenylmethane has hitherto usually been prepared by the interaction of benzene and chloroform in the presence of aluminium chloride [5] or ferric chloride,[2] but the yields are considerably lower. Other methods consist in the action of benzal chloride upon benzene and aluminium chloride,[6] in heating benzal chloride and mercury diphenyl,[7] and in heating a mixture of benzaldehyde, benzene, and zinc chloride.[8]

[1] Ber. **33**, 3147 (1900).
[2] Ber. **32**, 2422 (1899).
[3] J. Amer. Chem. Soc. **35**, 204 (1913).
[4] Ber. **45**, 3188 (1912).
[5] Ber. **14**, 1516 (1881); **26**, 1961 (1893); Bull. soc. chim. (2) **37**, 6 (1882); Ann. **227**, 108 (1885).
[6] Am. Chem. J. **13**, 556 (1891).
[7] Ber. **5**, 906 (1872).
[8] Ann. **242**, 329 (1887).

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